Access DB# [illegible]

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Margaret B Medley Examiner #: 60850 Date: 7-17-01
Art Unit: 1714 Phone Number 308-2518 Serial Number: 09/549,428 April 14, 2000
Mail Box and Bldg/Room Location: 3-3 Results Format Preferred (circle): PAPER DISK E-MAIL
3-4 D09

If more than one search is submitted, please prioritize searches in order needed.

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Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Process for the Separation of Enantiomers and Enantiopure Reagent

Inventors (please provide full names): Delplanche, Thierry et al

Earliest Priority Filing Date: _____

Search for the compds of Cls. 10-Band 18

For Sequence Searches Only *Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

Search c

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STAFF USE ONLY

Searcher: [illegible]	**Type of Search**		**Vendors and cost where applicable**
Searcher Phone #: X-4139	NA Sequence (#)		STN ✓
Searcher Location: EIC 1700	AA Sequence (#)		Dialog
Date Searcher Picked Up:	Structure (#)	(2)	Questel/Orbit
Date Completed: 7-19-01	Bibliographic		Dr.Link
Searcher Prep & Review Time: 55	Litigation		Lexis/Nexis
Clerical Prep Time: 15	Fulltext		Sequence Systems
Online Time: 65	Patent Family		WWW/Internet
	Other		Other (specify)

PTO-1590 (1-2000)

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L32        80299 SEA FILE=REGISTRY ABB=ON  PLU=ON  ?PHENYLALANIN?/CNS
L33         4672 SEA FILE=REGISTRY ABB=ON  PLU=ON  ?NITRO?/CNS (L) L32
L34          757 SEA FILE=REGISTRY ABB=ON  PLU=ON  N-4-NITRO? (L) L33
L35            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  2-METHOXY? (L) L34


=> d l35

L35  ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2001 ACS
RN   328406-65-1  REGISTRY
CN   L-Phenylalanine, N-[(4-nitrophenoxy)carbonyl]-, 2-methoxyethyl ester
     (9CI)  (CA INDEX NAME)
FS   STEREOSEARCH
MF   C19 H20 N2 O7
SR   CA
LC   STN Files:   CA, CAPLUS, TOXLIT

Absolute stereochemistry.
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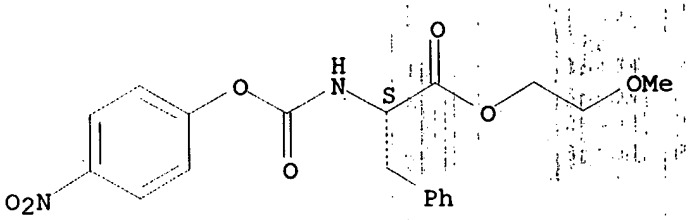


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                1 REFERENCES IN FILE CA (1967 TO DATE)
                1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

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Timothy Saunders EIC-LAW Lib. 308-413

L36 1 SEA FILE=REGISTRY ABB=ON PLU=ON 328406-65-1
L37 1 SEA FILE=HCAPLUS ABB=ON PLU=ON L36

=> d all hitstr l37

L37 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2001 ACS
AN 2001:57848 HCAPLUS
DN 134:212851
TI Application of (S)-N-(4-nitrophenoxycarbonyl) phenylalanine methoxyethyl ester as a new chiral derivatizing agent for proteinogenic amino acid analysis by high-performance liquid chromatography
AU Peter, A.; Vekes, E.; Torok, G.
CS Department of Inorganic and Analytical Chemistry, University of Szeged, Szeged, 6720, Hung.
SO Chromatographia (2000), 52(11/12), 821-826
CODEN: CHRGB7; ISSN: 0009-5893
PB Friedrich Vieweg & Sohn Verlagsgesellschaft mbH
DT Journal
LA English
CC 64-3 (Pharmaceutical Analysis)
AB The application of (S)-N-(4-nitrophenoxycarbonyl)phenylalanine methoxyethyl ester, (S)-NIFE, as a new chiral derivatizing agent for the resoln. of compds. possessing an amino group is described. Its applicability is demonstrated by the resoln. of proteinogenic amino acid enantiomers. The diastereomeric derivs. produced were sepd. by reversed-phase high-performance liq. chromatog. The effects of pH, excess reagent and reaction time on the derivatization kinetics, and the effects of pH and the org. modifier on the sepn., were investigated.
ST nitrophenoxycarbonyl phenylalanine deriv chiral agent HPLC; liq chromatog detn amino acid detn
IT HPLC
Reversed phase HPLC
(sepn. of amino acids by reversed phase HPLC using (S)-N-(4-nitrophenoxycarbonyl) phenylalanine methoxyethyl ester as chiral derivatizing agent)
IT 52-90-4, L-Cysteine, analysis 56-41-7, L-Alanine, analysis 56-45-1, L-Serine, analysis 56-84-8, L-Aspartic acid, analysis 56-85-9, L-Glutamine, analysis 56-86-0, L-Glutamic acid, analysis 56-87-1, L-Lysine, analysis 60-18-4, L-Tyrosine, analysis 61-90-5, L-Leucine, analysis 63-68-3, L-Methionine, analysis 63-91-2, L-Phenylalanine, analysis 70-47-3, L-Asparagine, analysis 71-00-1, L-Histidine, analysis 72-18-4, L-Valine, analysis 72-19-5, L-Threonine, analysis 73-22-3, L-Tryptophan, analysis 73-32-5, L-Isoleucine, analysis 74-79-3, L-Arginine, analysis 147-85-3, L-Proline, analysis 302837-19-0 302837-20-3 302837-22-5 302837-24-7 302837-25-8 302837-27-0 302837-29-2 302837-30-5 302837-31-6 302837-34-9 302837-35-0 302837-36-1 328406-66-2 328406-67-3 328406-68-4 328406-69-5 328406-70-8 328406-71-9 328406-72-0
RL: ANT (Analyte); ANST (Analytical study)
(sepn. of amino acids by reversed phase HPLC using (S)-N-(4-nitrophenoxycarbonyl) phenylalanine methoxyethyl ester as chiral derivatizing agent)
IT **328406-65-1**
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(sepn. of amino acids by reversed phase HPLC using (S)-N-(4-nitrophenoxycarbonyl) phenylalanine methoxyethyl ester as chiral derivatizing agent)
RE.CNT 11
RE

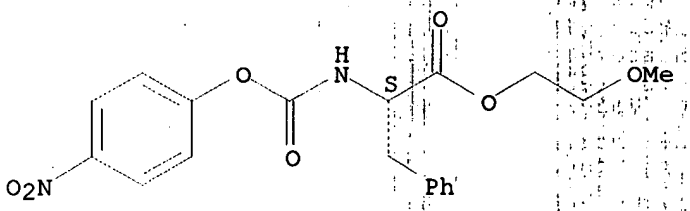
(1) Anon; J Biol Chem 1989, V264, P668
(2) Beesley, T; Chiral Chromatography 1998
(3) Bojarski, J; Chem Anal 1997, V42, P139 HCAPLUS
(4) Delplanche, T; Peptidomimetics Symposium 1999, 11
(5) Gorog, S; Chromatogr B 1994, V659, P51 MEDLINE
(6) Kleidernigg, O; Chromatographia 1997, V44, P465 HCAPLUS
(7) Lunn, G; Handbook of Derivatization Reactions for HPLC 1998
(8) Nimura, N; J Chromatogr 1980, V202, P375 HCAPLUS
(9) Okamoto, Y; Chromatographic Enantiomer Separation on Chiral Polymers 1997
(10) Solvay; patent pending
(11) Toyo'oka, T; Modern Derivatization Methods for Separation Science 1999

IT **328406-65-1**
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(sepn. of amino acids by reversed phase HPLC using (S)-N-(4-nitrophenoxycarbonyl) phenylalanine methoxyethyl ester as chiral derivatizing agent)

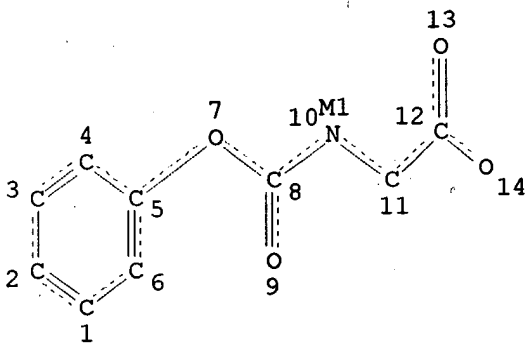
RN 328406-65-1 HCAPLUS

CN L-Phenylalanine, N-[(4-nitrophenoxy)carbonyl]-, 2-methoxyethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L1 STR



NODE ATTRIBUTES:
HCOUNT IS M1 AT 10
NSPEC IS R AT 1
NSPEC IS R AT 2
NSPEC IS R AT 3
NSPEC IS R AT 4
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NSPEC IS C AT 7
NSPEC IS C AT 8
NSPEC IS C AT 9
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NSPEC IS C AT 11
NSPEC IS C AT 12
NSPEC IS C AT 13
NSPEC IS C AT 14
DEFAULT MLEVEL IS ATOM
MLEVEL IS CLASS AT 7 8 9 10 11 12 13 14
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 14

STEREO ATTRIBUTES: NONE

L3	501	SEA FILE=REGISTRY SSS FUL L1
L4	213	SEA FILE=HCAPLUS ABB=ON PLU=ON L3
L6	1	SEA FILE=HCAPLUS ABB=ON PLU=ON 2000:755247/AN
L14	75483	SEA FILE=HCAPLUS ABB=ON PLU=ON (AMINO ACIDS OR PEPTIDES OR PROTEINS)/CC
L15	83	SEA FILE=HCAPLUS ABB=ON PLU=ON L4 AND L14
L16	82	SEA FILE=HCAPLUS ABB=ON PLU=ON L15 NOT L6
L18	4	SEA FILE=HCAPLUS ABB=ON PLU=ON (HPLC OR CHROMATOGARPH?) AND L16
L19	9	SEA FILE=HCAPLUS ABB=ON PLU=ON (ENANTIO? OR SEPARAT? OR CHROMOPHO? OR REAGENT) AND L16
L20	12	SEA FILE=HCAPLUS ABB=ON PLU=ON L18 OR L19

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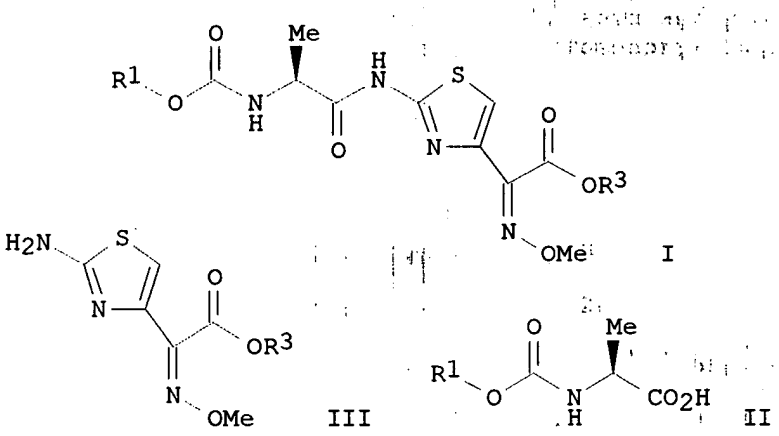
L20 ANSWER 1 OF 12 HCAPLUS COPYRIGHT 2001 ACS
AN 2001:220249 HCAPLUS
DN 134:237834
TI Method for preparation of 2-[[N-(hydrocarbyloxycarbonyl)-L-alanyl]amino]thiazole-4-acetic acid ester derivatives
IN Hirota, Yoshihiro; Matsunaga, Tomonori; Iwasaki, Fumiaki
PA Tokuyama Corp., Japan
SO Jpn. Kokai Tokkyo Koho, 12 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
IC ICM C07D277-44
CC 34-2 (**Amino Acids, Peptides,** and **Proteins**)
Section cross-reference(s): 1, 26
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001081083	A2	20010327	JP 1999-259786	19990914

OS CASREACT 134:237834; MARPAT 134:237834
GI



AB The title compds. (I; R1 = C1-6 alkyl, C6-8 aryl, CH2Ph; R2 = C1-6 alkyl, Ph, CH2Ph) are prepd. by condensation of N-(hydrocarbyloxycarbonyl)-L-alanine (II; R1 = same as above) with 2-(2-amino-5-thiazolyl)-2-methoxyiminoacetic acid ester (III; R2 = same as above) using a condensing agent, more specifically N,N'-carbonyldiimidazole and converted into 2-[2-[[N-(hydrocarbyloxycarbonyl)-L-alanyl]amino]thiazol-4-yl]-2-methoxyiminoacetic acid I (R1 = same as above; R2 = H) by hydrolysis in the presence of base and neutralization. The latter 2-(2-aminothiazol-4-yl)-2-methoxyiminoacetic acid derivs. are useful as intermediates for drugs, and in particular used as side chains for cephalosporin antibiotics. N,N'-carbonyldiimidazole is superior to other condensing agents such as dicyclohexylcarbodiimide and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride and gives I in high yields. This process also gives III with high purity, enables the skipping of purifn. step for III prior to sapon., and simplifies and significantly improves the prodn. efficiency for the sapond. product, i.e. free acid I (R1 = same as above; R2 = H). Thus, 47.3 g N-tert-butoxycarbonyl-L-

alanine and 57.3 g 2-(2-aminothiazol-4-yl)-2-(Z)-(methoxyimino)acetic acid Et ester were added to 250 mL EtOAc, cooled to 0.degree., treated slowly with 40.5 g N,N'-carbonyldiimidazole over a period of 10 min at .ltoreq.5.degree., and stirred at 4.degree. for 1 h. The reaction mixt. was washed with 2 N HCl twice and 2 N NaOH and the org. layer was **sepd**. to give, after evapn. of the solvent and silica gel chromatog., 90.4 g I (R1 = tert-Bu, R2 = Et) (90.0% yield). In a sapon. step, the org. layer obtained above was distd. in vacuo to the wt. of 113.2 g, treated with 67.2 g MeOH, and then slowly with 125 mL 3 N NaOH at .ltoreq.25.degree. over a period of 15 min, and allowed to react at 25.degree. for 5 h. The solvent was distd. in vacuo from the reaction mixt. until the mixt. weighed at 187.2 g, followed by adding 130 g H2O, and the resulting mixt. was cooled 7.degree., treated slowly with 260 mL 2 N HCl over a period of 1 h, and stirred at .ltoreq.5.degree. for 2 h to give, after centrifugation and washing the **sepd**. solid with water and drying, 81.1 g I (R1 = tert-Bu, R2 = H) (87.0% yield).

ST alanylaminothiazolylmethoxyiminoacetic acid ester prepn intermediate cephalosporin antibiotic; hydrocarbyloxycarbonylalanine condensation aminothiazolylmethoxyiminoacetic acid ester; methoxyiminoacetic acid ester alanyl aminothiazolyl prepn intermediate cephalosporin antibiotic

IT Condensation reaction
(prepn. of [[N-(hydrocarbyloxycarbonyl)-L-alanyl]amino]thiazoleacetic acid ester derivs. by condensation of N-(hydrocarbyloxycarbonyl)-L-alanine with (aminothiazolyl)methoxyiminoacetic acid ester using N,N'-carbonyldiimidazole)

IT Lactams
RL: PNU (Preparation, unclassified); PREP (Preparation)
(.beta.-, antibiotics; prepn. of [[N-(hydrocarbyloxycarbonyl)-L-alanyl]amino]thiazoleacetic acid ester derivs. by condensation of N-(hydrocarbyloxycarbonyl)-L-alanine with (aminothiazolyl)methoxyiminoacetic acid ester using N,N'-carbonyldiimidazole)

IT 530-62-1, N,N'-Carbonyldiimidazole 1142-20-7 15761-38-3 16639-86-4, N-Ethoxycarbonyl-L-alanine 33294-53-0 64485-88-7 65243-09-6
141695-27-4, N-Pheoxycarbonyl-L-alanine 162281-00-7
RL: RCT (Reactant)
(prepn. of [[N-(hydrocarbyloxycarbonyl)-L-alanyl]amino]thiazoleacetic acid ester derivs. by condensation of N-(hydrocarbyloxycarbonyl)-L-alanine with (aminothiazolyl)methoxyiminoacetic acid ester using N,N'-carbonyldiimidazole)

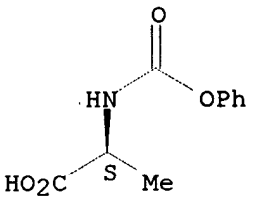
IT 330566-03-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of [[N-(hydrocarbyloxycarbonyl)-L-alanyl]amino]thiazoleacetic acid ester derivs. by condensation of N-(hydrocarbyloxycarbonyl)-L-alanine with (aminothiazolyl)methoxyiminoacetic acid ester using N,N'-carbonyldiimidazole)

IT 88970-81-4P 330566-04-6P 330566-05-7P 330566-06-8P 330566-07-9P 330566-08-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of [[N-(hydrocarbyloxycarbonyl)-L-alanyl]amino]thiazoleacetic acid ester derivs. by condensation of N-(hydrocarbyloxycarbonyl)-L-alanine with (aminothiazolyl)methoxyiminoacetic acid ester using N,N'-carbonyldiimidazole)

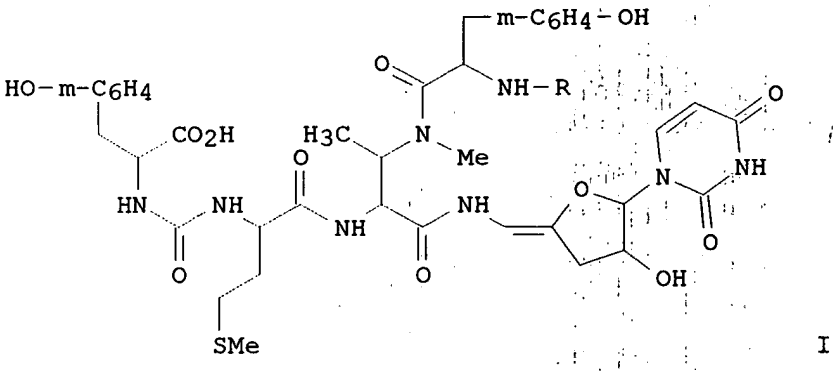
IT **141695-27-4**, N-Pheoxycarbonyl-L-alanine
RL: RCT (Reactant)
(prepn. of [[N-(hydrocarbyloxycarbonyl)-L-alanyl]amino]thiazoleacetic acid ester derivs. by condensation of N-(hydrocarbyloxycarbonyl)-L-alanine with (aminothiazolyl)methoxyiminoacetic acid ester using N,N'-carbonyldiimidazole)

RN 141695-27-4 HCAPLUS
CN L-Alanine, N-(phenoxycarbonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L20 ANSWER 2 OF 12 HCAPLUS COPYRIGHT 2001 ACS
AN 2000:853644 HCAPLUS
DN 134:193704
TI A solid-phase approach to analogues of the antibiotic mureidomycin
AU Bozzoli, Andrea; Kazmierski, Wieslaw; Kennedy, Gordon; Pasquarello, Alessandra; Pecunioso, Angelo
CS GlaxoWellcome SpA, Medicines Research Centre, Verona, 37135, Italy
SO Bioorg. Med. Chem. Lett. (2000), 10(24), 2759-2763
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
CC 34-3 (**Amino Acids, Peptides,** and **Proteins**)
Section cross-reference(s): 26, 33
GI



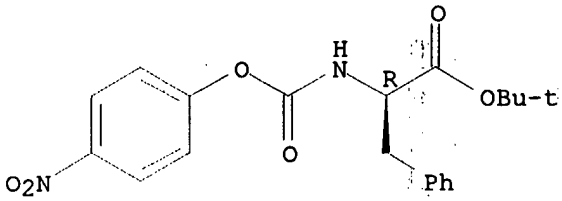
I

AB A library of 80 analogs of the antibacterial family of mureidomycins [(I); R = H, mureidomycin A; R = Gly, mureidomycin C], was prepd. using solid-phase chem. techniques. Analog fragments (2,3-diaminopropionic acid, methionine, p-tyrosine, m-tyrosine, as **enantiomers**, and tert-Bu 2-Ph malonate, as a racemate), were used in the synthesis. A selection of ten of the compds. with best a/a values (by LC-MS anal.) was presented. No inhibitory activity on the growth of S. aureus 853, E coli 1952, Saccharomyces cerevisiae NCY81, P. aeruginosa and P aeruginosa 2033 were detected for any library member.
ST mureidomycin analog combinatorial library prepn solid phase MSBAR
IT Combinatorial library
Solid phase synthesis
Structure-activity relationship
(prepn. of a combinatorial library of mureidomycin analogs using

solid-phase synthesis)
IT Natural products
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of a combinatorial library of mureidomycin analogs using solid-phase synthesis)
IT 114797-04-5DP, Mureidomycin A, analogs 327184-82-7P 327184-83-8P 327184-84-9P 327184-85-0P 327184-86-1P 327184-87-2P 327184-88-3P 327184-89-4P 327184-90-7P 327184-91-8P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of a combinatorial library of mureidomycin analogs using solid-phase synthesis)
IT 348-67-4, D-Methionine 362-43-6 673-06-3, D-Phenylalanine 7693-46-1 78342-42-4 109838-85-9 198544-42-2 **327184-80-5** 327184-92-9 327184-93-0
RL: RCT (Reactant)
(prepn. of a combinatorial library of mureidomycin analogs using solid-phase synthesis)
IT 15083-05-3P 15083-09-7P 68691-77-0P 265321-20-8P 327184-50-9P 327184-51-0P 327184-52-1P 327184-53-2DP, resin-bound 327184-53-2P 327184-54-3P 327184-55-4P 327184-56-5P 327184-57-6P 327184-58-7P 327184-59-8P 327184-60-1P 327184-61-2P 327184-62-3P 327184-63-4P 327184-64-5P 327184-65-6P 327184-66-7P 327184-67-8P 327184-68-9P **327184-69-0P 327184-70-3P** 327184-71-4DP, resin-bound 327184-72-5DP, resin-bound 327184-73-6DP, resin-bound 327184-76-9DP, resin-bound 327184-78-1DP, resin-bound 327184-79-2DP, resin-bound
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of a combinatorial library of mureidomycin analogs using solid-phase synthesis)
IT 327184-74-7P 327184-75-8P 327184-77-0P 327184-81-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of a combinatorial library of mureidomycin analogs using solid-phase synthesis)
RE.CNT 20
RE
(1) Armstrong, A; Tetrahedron Lett 1988, V29, P2483 HCAPLUS
(2) Brandish, P; Antimicrob Agents Chemother 1996, V40, P1640 HCAPLUS
(3) Brandish, P; J Biol Chem 1996, V271, P7609 HCAPLUS
(4) Bugg, T; J Chem Soc, Perkin Trans 1 1999, P1279
(5) Bugg, T; J Chem Soc, Perkin Trans 1 1999, P1285
(6) Chang, C; Int J Pept Protein Res 1980, V15, P59 HCAPLUS
(7) Inukai, M; Antimicrob Agents and Chemother 1993, V37, P980 HCAPLUS
(8) Isono, F; Antimicrob Agents Chemother 1991, V35, P234 HCAPLUS
(9) Isono, F; J Antibiot 1989, V42, P667 HCAPLUS
(10) Isono, F; J Antibiot 1989, V62, P674
(11) Kaiser, E; Anal Biochem 1970, V34, P595 HCAPLUS
(12) Lee, V; Med Res Rev 1999, V19, P521 HCAPLUS
(13) Merrifield, R; J Org Chem 1993, V58, P5167
(14) Niccolai, D; Chem Commun 1997, P2333 HCAPLUS
(15) Pedroso, E; Tetrahedron Lett 1993, V34, P2195
(16) Raju, B; Bioorg Med Chem Lett 1998, V8, P3043 HCAPLUS
(17) Roth, V; Emerging Therapeutic Targets 1999, V3, P73 HCAPLUS
(18) Schollkopf, U; Angew Chem, Int Ed Engl 1981, V20, P798
(19) Setti, E; Drugs Future 1997, V22, P271 HCAPLUS
(20) Williams, R; Synthesis of Optically Active .alpha.-Amino Acids 1989
IT **327184-80-5**
RL: RCT (Reactant)
(prepn. of a combinatorial library of mureidomycin analogs using solid-phase synthesis)

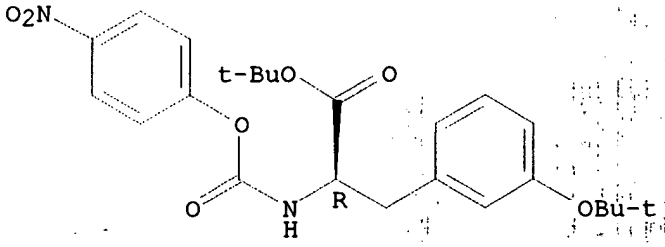
RN 327184-80-5 HCAPLUS
CN D-Phenylalanine, N-[(4-nitrophenoxy)carbonyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **327184-69-0P 327184-70-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of a combinatorial library of mureidomycin analogs using solid-phase synthesis)
RN 327184-69-0 HCAPLUS
CN D-Phenylalanine, 3-(1,1-dimethylethoxy)-N-[(4-nitrophenoxy)carbonyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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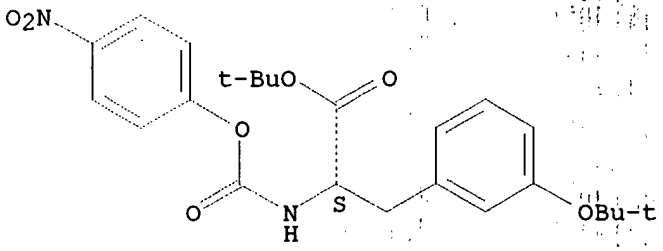
Absolute stereochemistry.



L20 ANSWER 3 OF 12 HCAPLUS COPYRIGHT 2001 ACS
AN 2000:421093 HCAPLUS
DN 133:43809
TI Preparation of new biphenyl and biphenyl-analogous compounds as integrin antagonists
IN Albers, Markus; Urbahns, Klaus; Vaupel, Andrea; Harter, Michael; Schmidt,

Delf; Stelte-ludwig, Beatrix; Gerdes, Christoph; Stahl, Elke; Keldenich, Jorg; Bruggemeier, Ulf; Lustig, Klemens

PA Bayer Aktiengesellschaft, Germany; et al.

SO PCT Int. Appl., 360 pp.
CODEN: PIXXD2

DT Patent

LA English

IC ICM C07C311-19
ICS C07C275-42; C07C311-10; C07C311-47; C07D213-40; C07D213-75; C07D235-30; A61K031-18; A61K031-44; A61K031-4184; A61P035-00; A61P019-10; A61P027-02

CC 34-2 (**Amino Acids, Peptides,** and **Proteins**)
Section cross-reference(s): 1, 25

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000035864	A1	20000622	WO 1999-EP9843	19991213

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 1998-213381 A 19981216

OS MARPAT 133:43809

AB Biphenylyl compds. R1O2CCHR2-U-V-A-B-W-NR3-C-R4 [R1 = H, (un)substituted alkyl, cycloalkyl, aryl, or (un)satd. heterocyclyl; R2 = H, (un)substituted alkyl, cycloalkyl, aryl, or (un)satd. heterocyclyl, alkenyl, alkynyl, -NR2'SO2R'', -NR2'CO2R2', -NR2'COR2', -NR2'CONR2'2, -NR2'CSNR2'2 (R2' has same definition as R1 and R2'' has same definition as R1 except it is not H); U or W is a direct bond or (un)substituted alkylene; V = (un)substituted alkylene, -NR2'CO- or NR2'SO2-; A and B = (un)substituted 1,3- or 1,4-bridging phenylene group or a 2,4- or 2,5-bridging thienylene group, each of which may have substituents; C is a direct bond, CMe(:X-R5)-Y-N(R6)- (R5 is absent, H, (un)substituted alkyl or cycloalkyl, NO2, acyl, carboxylic or carboxylate group or is connected to R3, Y, R4 or R6, if present; R6 is H, (un)substituted alkyl, cycloalkyl, aryl, or (un)satd. heterocyclyl, an alkylamine or alkylamide residue, or is connected to one of R3, R4, Y, or R5, if present, to form a heterocyclic ring system; X = CHNO2, CHCN, O, N or S; Y is a direct bond or (un)substituted alkylene or alkyne group) or 3,4-dioxo-1,2-cyclobutenediyl-NR6-; R3, R4 = H, (un)substituted alkyl, cycloalkyl, aryl, or (un)satd. heterocyclyl, an alkylamine or alkylamide residue, or is connected to one of R4 (or R3), Y, R5 or R6, if present, to form a heterocyclic ring system] were prepd. as integrin antagonists. Thus, (2R,S)-3-[3-(pyridin-3-ylmethylureido)biphenyl-4-yl]-2-[2,4,6-trimethylbenzenesulfonylamino]propanoic acid, prepd. by reactions of resin-bound (2R,S)-3-(4-bromophenyl)-2-(9-fluorenylmethoxycarbonylamino)propanoic acid with sulfonylating, boronic acid, and amine **reagents** (mesitylenesulfonyl chloride, 3-nitrobenzeneboronic acid, and 2-aminomethylpyridine), showed IC50 = 5 nM for binding to the .alpha.v.beta.3 receptor and IC50 = 480 nM in the smooth muscle cell migration test.

ST amino acid biphenylyl deriv prepn antagonist integrin

IT Angiogenesis
Antitumor agents

Arteriosclerosis
Eye, disease
Osteoporosis
Rheumatoid arthritis
(prepn. of new biphenyl and biphenyl-analogous compds. as integrin antagonists)

IT Amino acids, preparation
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of new biphenyl and biphenyl-analogous compds. as integrin antagonists)

IT Artery, disease
(restenosis; prepn. of new biphenyl and biphenyl-analogous compds. as integrin antagonists)

IT Integrins
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(.alpha.v.beta.3; prepn. of new biphenyl and biphenyl-analogous compds. as integrin antagonists)

IT 276257-75-1P 276257-76-2P 276257-77-3P 276257-78-4P 276257-79-5P
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276260-26-5P **276260-27-6P** 276260-28-7P 276260-29-8P
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276260-40-3P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of new biphenyl and biphenyl-analogous compds. as integrin antagonists)

IT 276260-41-4P 276260-42-5P 276260-43-6P 276260-44-7P 276260-45-8P
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276262-68-1P 276262-69-2P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of new biphenyl and biphenyl-analogous compds. as integrin antagonists)

IT 51-45-6, 2-(Imidazol-4-yl)ethylamine, reactions 78-81-9, Isobutylamine

88-14-2, 2-Furancarboxylic acid 96-15-1, 2-Methylbutylamine 96-50-4, 2-Aminothiazole 98-58-8, 4-Bromobenzenesulfonyl chloride 98-60-2, 4-Chlorobenzenesulfonyl chloride 107-15-3, 1,2-Ethanediamine, reactions 108-00-9, n,n-Dimethylethylenediamine 108-91-8, Cyclohexylamine, reactions 462-08-8, 3-Aminopyridine 504-24-5, 4-Aminopyridine 504-29-0, 2-Aminopyridine 645-36-3, Aminoacetaldehyde diethyl acetal 765-30-0, Cyclopropylamine 773-64-8, 2,4,6-Trimethylbenzenesulfonyl chloride 934-32-7, 2-Aminobenzimidazole 1001-53-2, n-Acetylethylenediamine 1003-03-8, Cyclopentylamine 2905-23-9, 2-Chlorobenzenesulfonyl chloride 2905-24-0, 3-Bromobenzenesulfonyl chloride 2991-42-6, 4-Trifluoromethylbenzenesulfonyl chloride 3731-51-9, 2-Aminomethylpyridine 3731-52-0, 3-Aminomethylpyridine 3731-53-1, 4-Aminomethylpyridine 4548-45-2, 2-Chloro-5-nitropyridine 4659-45-4, 2,6-Dichlorobenzoyl chloride 4795-29-3, 2-Aminomethyltetrahydrofuran 5231-87-8 5402-73-3, 2,5-Dichlorobenzenesulfonyl chloride 6335-76-8 7154-73-6, 2-Pyrrolidin-1-ylethylamine 7693-46-1, 4-Nitrophenyl chloroformate 10191-60-3, Dimethyl cyanimidodithiocarbonate 13258-63-4, 4-Pyridineethanamine 13331-27-6 13623-94-4 13952-84-6, sec-Butylamine 20781-20-8, 2,4-Dimethoxybenzylamine 21286-54-4, + Camphor 10 sulfonyl chloride 22374-89-6 23095-05-8, 5-Bromo-2-methoxybenzenesulfonyl chloride 29022-11-5, Fmoc gly oh 50998-05-5 66472-86-4 79711-73-2 79844-65-8 80500-27-2 87199-16-4, 3-Formylbenzeneboronic acid 87199-17-5, 4-Formylbenzeneboronic acid 88831-43-0 99359-32-7 107819-90-9 126727-04-6 180181-93-5 276262-70-5 276262-71-6
RL: RCT (Reactant)
(prepn. of new biphenyl and biphenyl-analogous compds. as integrin antagonists)

IT 276258-77-6P 276258-78-7P 276258-81-2P 276258-86-7P 276258-87-8P
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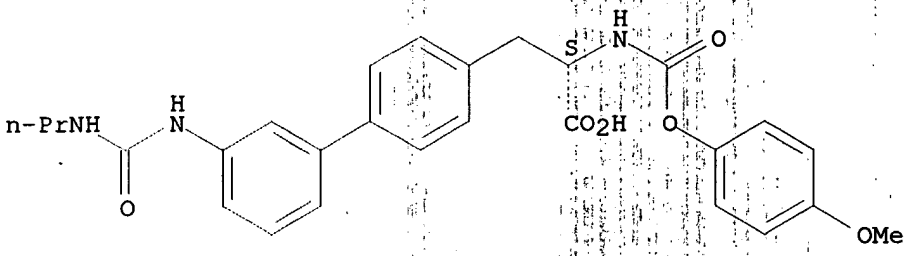
276259-19-9P 276259-20-2P 276259-21-3P 276259-23-5P 276259-24-6P
276259-25-7P 276262-72-7P 276262-73-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of new biphenyl and biphenyl-analogous compds. as integrin antagonists)

RE.CNT 4
RE
(1) Anon; WO 9736859 A 1997 HCAPLUS
(2) Merck, P; DE 19548709 A 1997 HCAPLUS
(3) Merck, P; WO 9800395 A 1998 HCAPLUS
(4) Tanabe, S; WO 9936393 A 1999 HCAPLUS

IT **276260-27-6P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of new biphenyl and biphenyl-analogous compds. as integrin antagonists)

RN 276260-27-6 HCAPLUS
CN [1,1'-Biphenyl]-4-propanoic acid, .alpha.-[[(4-methoxyphenoxy)carbonyl]amino]-3'-[[(propylamino)carbonyl]amino]-, (.alpha.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L20 ANSWER 4 OF 12 HCAPLUS COPYRIGHT 2001 ACS
AN 1999:584481 HCAPLUS
DN 132:12483
TI **Enantiomeric Separation** of (.+-.)-Amino Acid Esters on (-)-Phenylurea Chiral Stationary Phase
AU Lee, Kwang-Pill; Lee, Hyun-Bong; Lee, Young Cheol; Choi, Seong-Ho; Ryoo, Jae Jeong; Park, Jung Hag
CS Department of Chemistry, Graduate School, Kyungpook National University, Sangeok-dong, Taegu, 702-701, S. Korea
SO Microchem. J. (1999), 63(1), 18-23
CODEN: MICJAN; ISSN: 0026-265X
PB Academic Press
DT Journal
LA English
CC 34-2 (**Amino Acids, Peptides,** and **Proteins**)
Section cross-reference(s): 9
AB The 3,5-dinitrobenzoyl (.+-.)-amino acid esters were successfully resolved on (-)-phenylurea chiral stationary phases (CSPs) in a normal phase mode by high-performance liq. chromatog. (**HPLC**). The alcs. used for esterification were methanol, ethanol, and n-propanol. The effects of esterification were studied via retention and optical resoln. The solvent and its concn. effect on **enantioselectivity** have been investigated based on the binary or ternary solvent system. The alc. used in the binary or ternary solvent system was crit. to the **enantiomeric** resoln. of 3,5-dinitrobenzoyl amino acid esters while the nonalcoholic solvent was not suitable. The optical condition of the **enantiomeric** resoln. is discussed in terms of the solvent compn. and structure of the amino acid esters. The main chiral recognition mechanism based on the .pi.-.pi. interaction of the nitrobenzoyl group of the amino acid derivs. with the .pi.-basic Ph group of CSPs is described. (c) 1999 Academic Press.
ST amino acid ester **enantiomeric sepn** phenylurea chiral stationary phase; chromatog chiral stationary phase **sepn** amino acid ester **enantiomeric**
IT Chiral recognition
Chromatography
Esterification
Resolution (**separation**)
(**enantiomeric sepn.** of (.+-.)amino acid esters on (-)phenylurea chiral stationary phase)
IT Amino acids, preparation
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(**enantiomeric sepn.** of (.+-.)amino acid esters on (-)phenylurea chiral stationary phase)
IT 64-10-8, Phenylurea
RL: RCT (Reactant)
(chiral stationary phase for the resoln. of (.+-.)-amino acid esters)

IT 35519-07-4 74928-18-0 74928-20-4 74928-21-5 74928-22-6
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135088-79-8 135449-37-5 135449-39-7 138088-19-4 138088-20-7
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251538-64-4 **251538-65-5** 251538-66-6 251538-67-7
251538-68-8 251538-69-9 251538-70-2 **251538-71-3**
251538-72-4 251538-73-5
RL: RCT (Reactant)
(**enantiomeric sepn**. of on (-)phenylurea chiral stationary phase)
RE.CNT 13
RE
(1) Armstrong, D; J Chromatogr 1991, V539, P83 HCAPLUS
(2) Gisch, D; The 9th International Symposium on Column Liquid Chromatography 1985
(3) Keith, J; Chirality 1993, V5, P201
(4) Lam, S; J Chromatogr Sci 1984, V22, P416 HCAPLUS
(5) Okamoto, Y; Bull Chem Soc Jpn 1990, V63, P955 HCAPLUS
(6) Okamoto, Y; Chem Lett 1987, P1857 HCAPLUS
(7) Okamoto, Y; Chemtech 1988, P176 HCAPLUS
(8) Okamoto, Y; J Chromatogr 1986, V363, P173 HCAPLUS
(9) Pirkle, W; J Am Chem Soc 1987, V109, P5975 HCAPLUS
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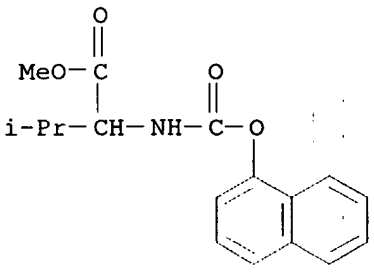
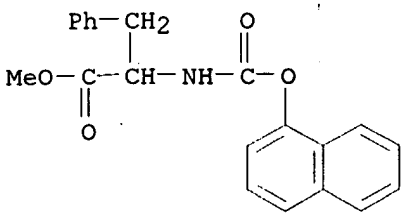
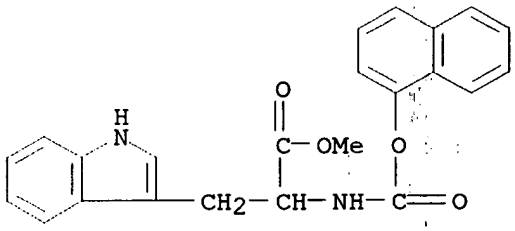
(11) Pirkle, W; J Org Chem 1992, V57, P3854 HCAPLUS
(12) Ryu, J; Anal Sci 1997, V13, P217 HCAPLUS
(13) Ryu, J; J Chromatogr A 1998, V14, P247
IT **251538-65-5 251538-68-8 251538-71-3**
RL: RCT (Reactant)
(**enantiomeric sepn**. of on (-)phenylurea chiral stationary phase)
RN 251538-65-5 HCAPLUS
CN Valine, N-[(1-naphthalenyloxy)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 251538-68-8 HCAPLUS
CN Phenylalanine, N-[(1-naphthalenyloxy)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



RN 251538-71-3 HCAPLUS
CN Tryptophan, N-[(1-naphthalenyloxy)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



L20 ANSWER 5 OF 12 HCAPLUS COPYRIGHT 2001 ACS
AN 1999:35812 HCAPLUS
DN 130:153966
TI Solid-phase synthesis of tyrosine peptide aldehydes. Analogs of (S)-MAPI
AU Page, Patrick; Bradley, Mark; Walters, Iain; Teague, Simon
CS Department of Chemistry, University of Southampton, Southampton, SO17 1BJ, UK
SO J. Org. Chem. (1999), 64(3), 794-799
CODEN: JOCEAH; ISSN: 0022-3263
PB American Chemical Society
DT Journal
LA English
CC 34-3 (**Amino Acids, Peptides,** and **Proteins**)
Section cross-reference(s): 1
AB We report an efficient solid-phase synthesis of C-terminal tyrosine peptide aldehydes based on the HIV protease inhibitors (S)-MAPI and GE 20372 A. Our strategy consisted of anchoring the side chain of Dde-Tyrosinol onto the brominated Wang linker deriv. ((4-bromomethyl)-phenoxy-allyl acetate) to give after ester hydrolysis the N.alpha.-(Dde)-O-(4-methylphenoxyacetic acid)-L-Tyrosinol template. This was attached to aminomethyl resin and elongated using std. Fmoc protocols. Importantly there was no evidence of esterification side reactions. The unsym. substituted urea linkage of the (S)-MAPI family was incorporated using the N.alpha.-(4-nitrophenyloxycarbonyl)amino acid tert-Bu esters following which the protected tetrapeptide alc. immobilized on the solid support was oxidized to its corresponding aldehyde using sulfur trioxide-pyridine. The efficiency and reliability of the oxidn. step was dramatically improved by the incorporation of a small PEG-spacer between the linker and the solid support. The tetrapeptides were cleaved by acidolysis, purified by RP **HPLC**, and isolated in high yield and purity, demonstrating the success of the whole synthetic process.
ST solid phase synthesis tyrosine peptide aldehyde oxidn
IT Peptides, preparation
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic

preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(aldehydes; solid-phase synthesis of tyrosine peptide aldehydes)

IT Oxidation
Solid phase synthesis
(solid-phase synthesis of tyrosine peptide aldehydes)

IT 70857-49-7P 163565-75-1P, GE 20372a
RL: BAC (Biological activity or effector, except adverse); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(solid-phase synthesis of tyrosine peptide aldehydes)

IT 220237-27-4P 220237-28-5P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(solid-phase synthesis of tyrosine peptide aldehydes)

IT 14221-01-3
RL: CAT (Catalyst use); USES (Uses)
(solid-phase synthesis of tyrosine peptide aldehydes)

IT 693-13-0, Diisopropyl carbodiimide 7087-68-5, Diisopropyl ethylamine 7446-11-9, Sulfur trioxide, reactions 13887-98-4 57260-73-8 155505-56-9 187526-99-4 **191425-55-5 191426-93-4**
RL: RCT (Reactant)
(solid-phase synthesis of tyrosine peptide aldehydes)

IT 220237-29-6DP, resin-bound 220237-30-9P 220237-31-0P 220237-32-1P 220237-33-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(solid-phase synthesis of tyrosine peptide aldehydes)

RE.CNT 38

RE

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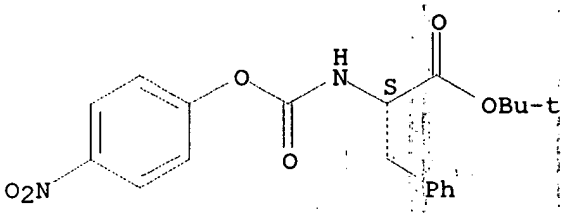
IT **191425-55-5 191426-93-4**
RL: RCT (Reactant)
(solid-phase synthesis of tyrosine peptide aldehydes)

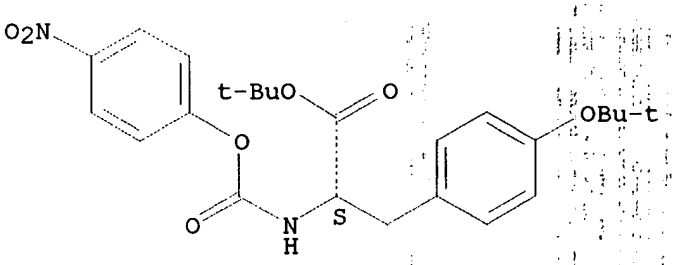
RN 191425-55-5 HCAPLUS
CN L-Phenylalanine, N-[(4-nitrophenoxy)carbonyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

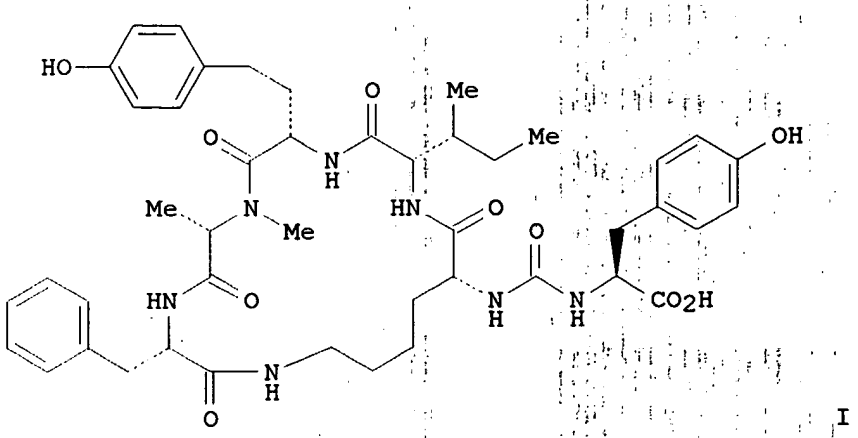


RN 191426-93-4 HCAPLUS
CN L-Tyrosine, O-(1,1-dimethylethyl)-N-[(4-nitrophenoxy)carbonyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L20 ANSWER 6 OF 12 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:598126 HCAPLUS
DN 127:176703
TI Solid-Phase Total Synthesis of Oscillamide Y and Analogs
AU Marsh, Ian R.; Bradley, Mark; Teague, Simon J.
CS Department of Chemistry, University of Southampton, Southampton, SO17 1BJ, UK
SO J. Org. Chem. (1997), 62(18), 6199-6203
CODEN: JOCEAH; ISSN: 0022-3263
PB American Chemical Society
DT Journal
LA English
CC 34-3 (**Amino Acids, Peptides,** and **Proteins**)
GI



I

AB An efficient solid phase synthesis of oscillamide Y (I) and three analogs is reported. The cyclic peptide was prepd. using a combination of 9-fluorenylmethoxycarbonyl (Fmoc) and allyl chemistries and an acid labile Wang type linker. The urea functionality was smoothly incorporated using D-lysine building block 4-O2NC6H4O2C-D-Lys(Fmoc)-OCH2CH:CH2. Coupling to the N-Me amino acid was readily achieved using HATU, monitoring the reaction using bromophenol blue. Allyl deprotection was accomplished using Pd(PPh3)4 and dimedone, and cyclization was smoothly accomplished using PyBroP. All reactions were monitored using mass spectrometry methodol. The cyclized materials were cleaved by acidolysis and purified by RP **HPLC**. In all cases the material isolated was the major product and gave the expected mol. ion information. **HPLC** comparison with an authentic sample of oscillamide Y showed that the isomer contg. N-methyl-L-alanine and L-homotyrosine was the natural product. 1H NMR and 1H-1H COSY NMR expts. further confirmed this identification. The four compds. were tested as competitive and slow-tight binding inhibitors of chymotrypsin but showed, contrary to literature expectations, no inhibitory activity.

ST oscillamide Y isomer solid phase synthesis

IT Solid phase peptide synthesis
(solid-phase total synthesis of oscillamide Y and analogs)

IT 68858-21-9, 4-(Hydroxymethyl)phenoxyacetic acid
RL: RCT (Reactant)
(handle; solid-phase total synthesis of oscillamide Y and analogs)

IT 34404-32-5, D-Lysine, N6-[(phenylmethoxy)carbonyl]-
RL: RCT (Reactant)
(solid-phase total synthesis of oscillamide Y and analogs)

IT 55878-47-2P 115186-31-7P, Boc-D-Lys(Fmoc)-OH 193948-47-9P
193948-49-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(solid-phase total synthesis of oscillamide Y and analogs)

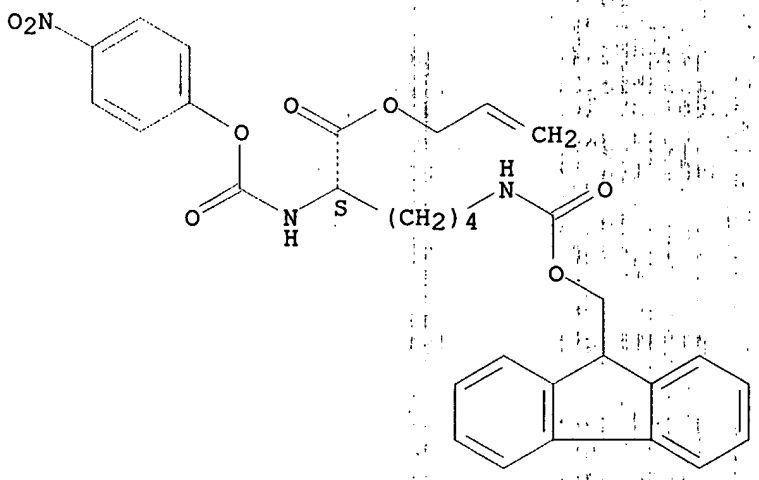
IT 168482-80-2P, Oscillamide Y 194038-14-7P 194038-15-8P 194038-16-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(solid-phase total synthesis of oscillamide Y and analogs)

IT **193948-49-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(solid-phase total synthesis of oscillamide Y and analogs)

RN 193948-49-1 HCAPLUS

CN L-Lysine, N6-[(9H-fluoren-9-ylmethoxy)carbonyl]-N2-[(4-nitrophenoxy)carbonyl]-, 2-propenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

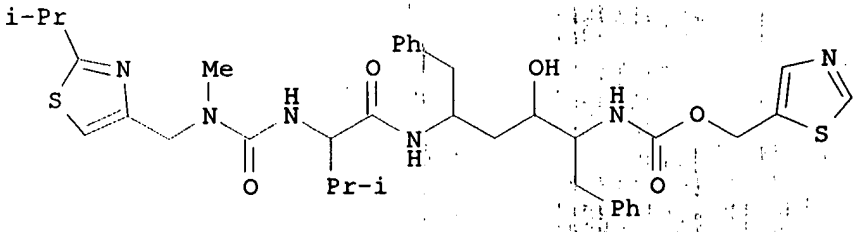


L20 ANSWER 7 OF 12 HCAPLUS COPYRIGHT 2001 ACS
AN 1996:610346 HCAPLUS
DN 125:301598
TI A solid pharmaceutical composition providing improved oral bioavailability for HIV protease inhibitors
IN Al-razzak, Laman A.; Marsh, Kennan C.; Pyter, Richard A.
PA Abbott Laboratories, USA
SO U.S., 18 pp. Cont.-in-part of U.S. Ser. No. 267,273,abandoned.
CODEN: USXXAM
DT Patent
LA English
IC ICM A61K031-16
ICS A61K031-695; A61K031-425; A61K031-42
NCL 514616000
CC 34-2 (**Amino Acids, Peptides,** and **Proteins**)
Section cross-reference(s): 63
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5559158	A	19960924	US 1994-297004	19940831
	CA 2167413	AA	19950413	CA 1994-2167413	19940909
	WO 9509614	A1	19950413	WO 1994-US10096	19940909
	W: AU, CA, JP, KR				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9477229	A1	19950501	AU 1994-77229	19940909
	AU 685509	B2	19980122		
	EP 721330	A1	19960717	EP 1994-928043	19940909
	EP 721330	B1	20010328		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	JP 09503501	T2	19970408	JP 1994-510810	19940909
	AT 200023	E	20010415	AT 1994-928043	19940909
	IL 110915	A1	19991222	IL 1994-110915	19940911
	US 5610193	A	19970311	US 1996-650261	19960522
PRAI	US 1993-130409	B2	19931001		
	US 1994-267273	B2	19940628		
	US 1994-297004	A	19940831		
	WO 1994-US10096	W	19940909		
	US 1995-424740	B1	19950418		

OS MARPAT 125:301598

GI



I

AB A solid pharmaceutical compn. is claimed, comprising a pharmaceutically acceptable adsorbent or a mixt. of pharmaceutically acceptable adsorbents to which is adsorbed a mixt. of (1) a pharmaceutically acceptable org. solvent or a mixt. of pharmaceutically acceptable org. solvents, (2) HIV protease inhibitor I, and (3) a pharmaceutically acceptable acid or a combination of pharmaceutically acceptable acids. Thus, e.g., a capsule compn. contg. (% by wt.): (all-S)-I = (2S,3S,5S)-5-[N-[N-[[N-methyl-N-[(2-isopropyl-4-thiazolyl)methyl]amino]carbonyl]valinyl]amino]-2-[N-[(5-thiazolyl)methoxycarbonyl]amino]-1,6-diphenyl-3-hydroxyhexane (prepn. given) (21.84); propylene glycol, USP (10.96); Ethanol, dehydrated USP, 200 proof (22.99); polysorbate 80, NF (5.31); Cremophor EL (4.4); HCl, **reagent** grade (1.18); Cab-o-sil (26.88) exhibited 89.6 mean % oral bioavailability in dogs vs. <2.0 for unformulated (all-S)-I in capsules.

ST oral pharmaceutical dosage HIV protease inhibitor

IT Acquired immune deficiency syndrome
(solid pharmaceutical compn. providing improved oral bioavailability for HIV protease inhibitors)

IT Castor oil
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ethoxylated, component of pharmaceutical formulation; solid pharmaceutical compn. providing improved oral bioavailability for HIV protease inhibitors)

IT Pharmaceutical dosage forms
(oral, solid pharmaceutical compn. providing improved oral bioavailability for HIV protease inhibitors)

IT 50-81-7, Ascorbic acid, biological studies 57-55-6, Propylene glycol, biological studies 64-17-5, Ethanol, biological studies 104-15-4, p-Toluenesulfonic acid, biological studies 7631-86-9, Silicon dioxide, biological studies 7647-01-0, Hydrochloric acid, biological studies 9005-65-6, Polysorbate 80 14807-96-6, Talc, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(component of pharmaceutical formulation; solid pharmaceutical compn. providing improved oral bioavailability for HIV protease inhibitors)

IT 9004-34-6, Cellulose, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(microcryst., component of pharmaceutical formulation; solid pharmaceutical compn. providing improved oral bioavailability for HIV protease inhibitors)

IT 162990-01-4P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(solid pharmaceutical compn. providing improved oral bioavailability for HIV protease inhibitors)

IT 144114-21-6, Retropepsin
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL

(Biological study)
(solid pharmaceutical compn. providing improved oral bioavailability for HIV protease inhibitors)

IT 143838-10-2P 144164-10-3P
RL: BYP (Byproduct); PREP (Preparation)
(solid pharmaceutical compn. providing improved oral bioavailability for HIV protease inhibitors)

IT 75-12-7, Formamide, reactions 105-39-5, Ethyl chloroacetate 534-07-6, 1,3-Dichloroacetone 563-83-7, Isobutyramide 6306-52-1, L-Valine methyl ester hydrochloride 6372-14-1, N-(Benzyloxycarbonyl)-L-phenylalaninol 7693-46-1, 4-Nitrophenyl chloroformate 24424-99-5, Di-tert-butyl dicarbonate **153441-77-1** 156732-13-7 156732-15-9
RL: RCT (Reactant)
(solid pharmaceutical compn. providing improved oral bioavailability for HIV protease inhibitors)

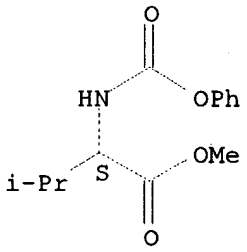
IT 115-08-2P, Thioformamide 13515-65-6P, Thioisobutyramide 32955-21-8P, 2-Amino-5-(ethoxycarbonyl)thiazole 32955-22-9P, Ethyl thiazole-5-carboxylate 33142-21-1P, Ethyl 2-chloro-2-formylacetate 38585-74-9P, 5-(Hydroxymethyl)thiazole 59830-60-3P, N-(Benzyloxycarbonyl)-L-phenylalaninal 65386-28-9P, 4-(Chloromethyl)-2-isopropylthiazole hydrochloride 137649-69-5P 144141-68-4P 144163-43-9P 144163-44-0P 144163-85-9P 144163-97-3P 144164-11-4P 154212-59-6P 154212-60-9P 154212-61-0P 154248-99-4P **162537-10-2P**, N-(4-Nitrophenoxycarbonyl)-L-valine Methyl Ester 162849-92-5P 162849-93-6P 162849-94-7P 162849-95-8P 162849-96-9P 162990-03-6P 165315-39-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(solid pharmaceutical compn. providing improved oral bioavailability for HIV protease inhibitors)

IT 155213-67-5P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(solid pharmaceutical compn. providing improved oral bioavailability for HIV protease inhibitors)

IT **153441-77-1**
RL: RCT (Reactant)
(solid pharmaceutical compn. providing improved oral bioavailability for HIV protease inhibitors)

RN 153441-77-1 HCAPLUS
CN L-Valine, N-(phenoxycarbonyl)-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

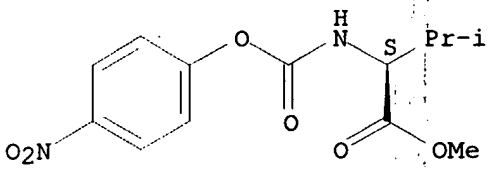


IT **162537-10-2P**, N-(4-Nitrophenoxycarbonyl)-L-valine Methyl Ester
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(solid pharmaceutical compn. providing improved oral bioavailability for HIV protease inhibitors)

RN 162537-10-2 HCAPLUS
CN L-Valine, N-[(4-nitrophenoxy)carbonyl]-, methyl ester (9CI) (CA INDEX

NAME)

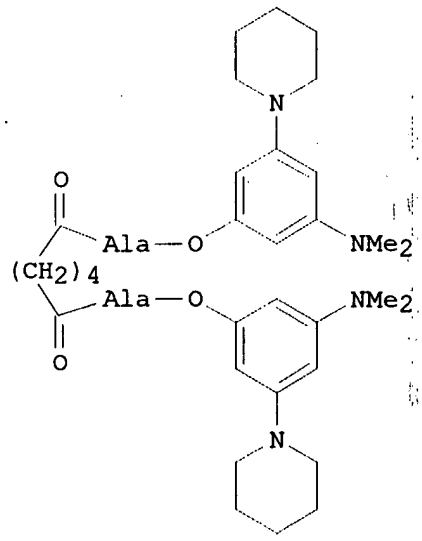
Absolute stereochemistry.



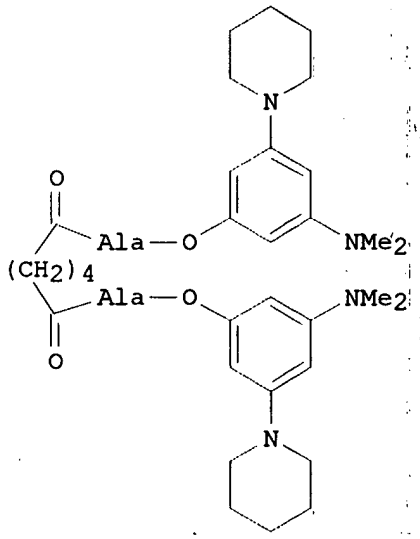
L20 ANSWER 8 OF 12 HCAPLUS COPYRIGHT 2001 ACS
AN 1995:928117 HCAPLUS
DN 123:340946
TI Novel amino acid ester and **reagent** composition for detecting leukocytes or elastase in bodily fluids.
IN Yagi, Yuji
PA Kyoto Daiichi Kagaku Co., Ltd., Japan
SO Eur. Pat. Appl., 19 pp.
CODEN: EPXXDW
DT Patent
LA English
IC ICM C07D295-12
ICS C07D213-81; C07D213-82; C07D307-68; C07D209-36; C07D213-64; C07D311-46; C07C311-19; C07D309-32; C12Q001-44
CC 34-2 (**Amino Acids, Peptides,** and **Proteins**)
Section cross-reference(s): 7, 9, 80
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 661280	A1	19950705	EP 1994-120650	19941224
R: CH, DE, FR, GB, IT, LI				
JP 07233131	A2	19950905	JP 1994-319986	19941222

PRAI JP 1993-349879 19931229
OS MARPAT 123:340946
GI



I



I

AB Amino acid esters of formula (XOA)nY [X = arom. or heterocyclic moiety; A = L-amino acid; n .gtoreq. 2; Y = moiety derived from compd. with 2 or more carbonyl or sulfonyl groups, bound to N of amino acid groups A] are claimed. The esters are hydrolyzed by leukocytes or elastase with high specificity, and are thus useful for detecting these in bodily fluids. For example, reaction of ClCO(CH2)4COCl (adipoyl dichloride) with excess L-alanine and pyridine gave 87.5% (CH2)4[CO-Ala-OH]2. This was treated with SOCl2 to give its acid dichloride (100%), which reacted with 3-(dimethylamino)-5-piperidinophenol [prepn. given] to give 65.8% title compd. I. A test paper based on I and 1-diazo-2-naphthol-4-sulfonic acid gave color change (red-purple) for leukocyte liq. or elastase, but no change for .alpha.-chymotrypsin, trypsin, cathepsin, or butylcholinesterase, and only slight change for subtilisin. Thirty syntheses and a variety of diagnostic examples are provided.

ST amino acid ester detn leukocyte elastase

IT Diagnosis
Leukocyte
Urine
(prepn. of amino acid esters as **reagents** for detecting leukocytes and elastase in bodily fluids)

IT Amino acids, preparation
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(esters, prepn. of amino acid esters as **reagents** for detecting leukocytes and elastase in bodily fluids)

IT 480-93-3P, 3-Hydroxyindole 13170-66-6P, Cyclohexane-1,4-dicarbonyl chloride 40248-00-8P 136458-21-4P 141187-06-6P 170487-71-5P 170487-72-6P 170487-73-7P 170487-74-8P 170487-75-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(intermediate; prepn. of amino acid esters as **reagents** for detecting leukocytes and elastase in bodily fluids)

IT 9004-06-2, Elastase
RL: ANT (Analyte); ANST (Analytical study)
(prepn. of amino acid esters as **reagents** for detecting leukocytes and elastase in bodily fluids)

IT 170487-41-9P 170487-42-0P 170487-43-1P 170487-44-2P 170487-45-3P 170487-46-4P 170487-47-5P **170487-48-6P** 170487-49-7P

170487-50-0P 170487-51-1P 170487-52-2P 170487-53-3P 170487-54-4P
170487-55-5P 170487-56-6P 170487-57-7P 170487-58-8P 170487-59-9P
170487-60-2P 170487-61-3P 170487-62-4P 170487-63-5P 170487-64-6P
170487-65-7P 170487-66-8P 170487-67-9P 170487-68-0P 170487-69-1P
170487-70-4P
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of amino acid esters as **reagents** for detecting leukocytes and elastase in bodily fluids)

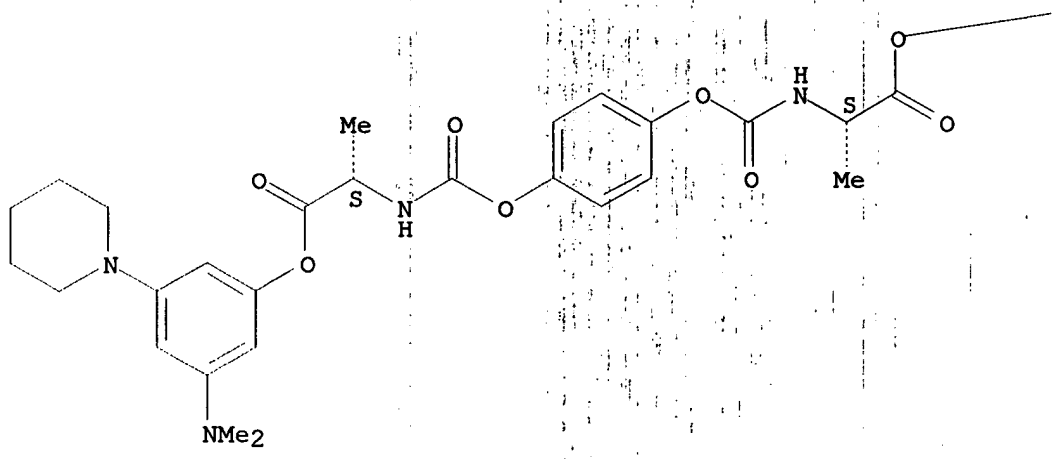
IT 56-40-6, Glycine, reactions 56-41-7, L-Alanine, reactions 61-90-5, L-Leucine, reactions 72-18-4, L-Valine, reactions 83-72-7, 2-Hydroxy-1,4-naphthoquinone 89-05-4, Benzene-1,2,4,5-tetracarboxylic acid 89-32-7 99-14-9, Propane-1,2,3-tricarboxylic acid 100-20-9, 1,4-Benzenedicarbonyl dichloride 108-73-6, 1,3,5-Trihydroxybenzene 110-89-4, Piperidine, reactions 111-50-2, Adipoyl chloride 119-80-2, 2,2'-Dithiodibenzoic acid 124-40-3, reactions 142-08-5, 2-Hydroxypyridine 533-75-5, Tropolone 585-47-7, Benzene-1,3-disulfonyl chloride 608-08-2, Indoxyl acetate 636-78-2, 4-Sulfobenzoic acid 1076-38-6, 4-Hydroxycoumarin 1076-97-7, 1,4-Cyclohexanedicarboxylic acid 1141-38-4, Naphthalene-2,6-dicarboxylic acid 3119-64-0, Diphenylmethane-4,4'-disulfonyl chloride 3387-26-6, Furan-3,4-dicarboxylic acid 3739-94-4, Pyridine-2,6-dicarbonyl chloride 4808-48-4 13827-62-8, Naphthalene-2,6-disulfonyl chloride 15658-35-2, 6,6'-Dithiodinicotinic acid 33177-29-6 67294-61-5, 1,3,6-Naphthalenetrisulfonyl chloride 170487-76-0 170487-77-1 170487-78-2 170487-79-3 170487-80-6
RL: RCT (Reactant)
(starting material; prepn. of amino acid esters as **reagents** for detecting leukocytes and elastase in bodily fluids)

IT **170487-48-6P**
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of amino acid esters as **reagents** for detecting leukocytes and elastase in bodily fluids)

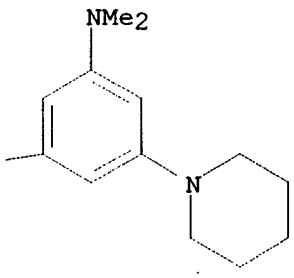
RN 170487-48-6 HCAPLUS
CN L-Alanine, N,N'-[1,4-phenylenebis(oxycarbonyl)]bis-, bis[3-(dimethylamino)-5-(1-piperidinyl)phenyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



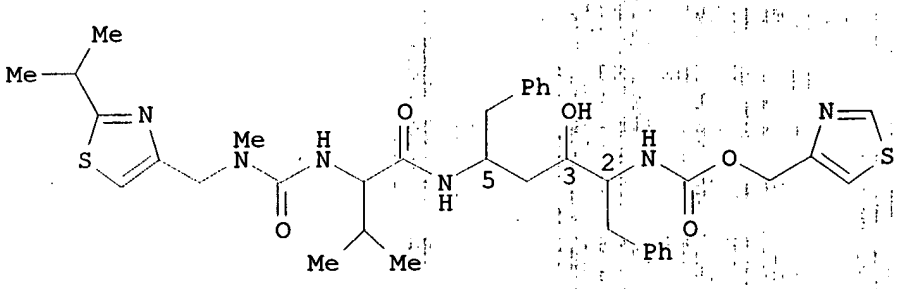
PAGE 1-B



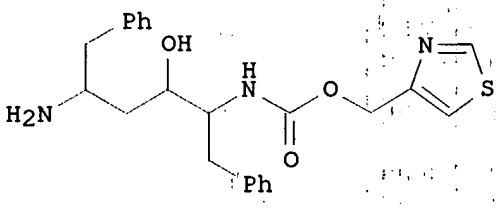
L20 ANSWER 9 OF 12 HCAPLUS COPYRIGHT 2001 ACS
AN 1995:887807 HCAPLUS
DN 123:314522
TI Pharmaceutical composition for HIV protease inhibitor [ritonavir] with improved oral bioavailability
IN Al-razzak, Laman A.; Marsh, Kennan C.; Pyter, Richard A.
PA Abbott Laboratories, USA
SO PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K009-14
ICS A61K009-16; A61K009-48
CC 34-2 (**Amino Acids, Peptides,** and **Proteins**)
Section cross-reference(s): 28, 63
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI WO 9509614 A1 19950413 WO 1994-US10096 19940909
W: AU, CA, JP, KR
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
US 5559158 A 19960924 US 1994-297004 19940831
AU 9477229 A1 19950501 AU 1994-77229 19940909
AU 685509 B2 19980122
EP 721330 A1 19960717 EP 1994-928043 19940909
EP 721330 B1 20010328
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE
JP 09503501 T2 19970408 JP 1994-510810 19940909
AT 200023 E 20010415 AT 1994-928043 19940909
PRAI US 1993-130409 A 19931001
US 1994-267273 A 19940628
US 1994-297004 A 19940831
WO 1994-US10096 W 19940909
OS MARPAT 123:314522
GI



I



II

AB A solid pharmaceutical compn. is disclosed which comprises a pharmaceutically acceptable adsorbent or mixt. of adsorbents, to which is adsorbed a mixt. of: (1) a pharmaceutically acceptable org. solvent or mixt. of solvents; (2) an HIV protease-inhibiting compd.; and (3) one or more pharmaceutically acceptable acids. The solid compn. can optionally be encapsulated in a hard gelatin capsule. The compn. is particularly applicable to compd. I, and esp. its (2S,3S,5S,L)-isomer [ritonavir; II]. For example, oral administration of unformulated II to dogs gave < 2.0% mean bioavailability. In contrast, 89.6% mean bioavailability was obtained with the following capsule formulation: II 21.84, propylene glycol 10.96, ethanol 22.99, Polysorbate 80 5.31, Cremophor EL 4.4, HCl 1.18, and Cab-o-sil 26.88% by wt. Also described are addnl. oral formulations (comparative and invention), and several syntheses of II. For example, N-(benzyloxycarbonyl)-L-phenylalaninol was converted in 5 steps to (2S,3S,5S)-PhCH2CH(NHZ)CH(OH)CH2CH(NHZ)CH2Ph [Z = benzyloxycarbonyl], which was deprotected and reacted with 5-thiazolylmethyl nitrophenyl carbonate to give intermediate III and its isomer from acylation of the other amino group. Coupling of III with N-[[N-methyl-N-[(2-isopropyl-4-thiazolyl)methyl]amino]carbonyl]-L-valine

[prepn. given] using the carbodiimide **reagent** EDC and 1-hydroxybenzotriazole gave II.

ST HIV protease inhibitor ritonavir pharmaceutical bioavailability; oral bioavailability HIV protease inhibitor

IT Drug bioavailability
Virucides and Virustats
(pharmaceutical compn. of HIV protease inhibitor with improved oral bioavailability)

IT Castor oil
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ethoxylated, Cremophor EL, adjuvant; pharmaceutical compn. of HIV protease inhibitor with improved oral bioavailability)

IT Pharmaceutical dosage forms
(oral, pharmaceutical compn. of HIV protease inhibitor with improved oral bioavailability)

IT 144114-21-6, Retropepsin
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(HIV-1 and HIV-2; pharmaceutical compn. of HIV protease inhibitor with improved oral bioavailability)

IT 50-81-7, Ascorbic acid, biological studies 57-55-6, Propylene glycol, biological studies 64-17-5, Ethanol, biological studies 77-92-9, Citric acid, biological studies 104-15-4, p-Toluenesulfonic acid, biological studies 7631-86-9, Silica, biological studies 7647-01-0, Hydrochloric acid, biological studies 9002-96-4 9004-34-6, Cellulose, biological studies 9005-25-8, Corn starch, biological studies 9005-65-6, Polysorbate 80 9050-36-6, Maltodextrin 14807-96-6, Talc, biological studies 41080-67-5
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adjuvant; pharmaceutical compn. of HIV protease inhibitor with improved oral bioavailability)

IT 115-08-2P, Thioformamide 13515-65-6P, 2-Methylpropanethioamide 32955-21-8P, 2-Amino-5-(ethoxycarbonyl)thiazole 32955-22-9P, Ethyl thiazole-5-carboxylate 33142-21-1P, Ethyl 2-chloro-2-formylacetate 38585-74-9P, 5-(Hydroxymethyl)thiazole 59830-60-3P, N-[[(Benzyl)oxy]carbonyl]-L-phenylalaninal 65386-28-9P, 4-(Chloromethyl)-2-isopropylthiazole hydrochloride 137649-69-5P 143838-10-2P 144141-68-4P 144163-43-9P 144163-44-0P 144163-85-9P 144163-97-3P 144164-10-3P 144164-11-4P 154212-59-6P 154212-60-9P, 2-Isopropyl-4-[(N-methylamino)methyl]thiazole 154212-61-0P 154248-99-4P **162537-10-2P** 162849-92-5P 162849-93-6P 162849-94-7P 162849-95-8P 162849-96-9P 162990-03-6P 165315-39-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(intermediate; pharmaceutical compn. of HIV protease inhibitor with improved oral bioavailability)

IT 155213-67-5P 162990-01-4P
RL: BPR (Biological process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(pharmaceutical compn. of HIV protease inhibitor with improved oral bioavailability)

IT 62-56-6, Thiourea, reactions 74-89-5, Methylamine, reactions 75-12-7, Formamide, reactions 98-80-6, Phenylboronic acid 105-39-5, Ethyl chloroacetate 109-94-4, Ethyl formate 534-07-6, 1,3-Dichloroacetone 563-83-7, Isobutyramide 6306-52-1, L-Valine methyl ester hydrochloride 6372-14-1, N-[[(Benzyl)oxy]carbonyl]-L-phenylalaninol 7693-46-1, 4-Nitrophenyl chloroformate 24424-99-5, Di-tert-butyl dicarbonate 40635-67-4, .alpha.-Acetoxyisobutyryl bromide **126147-70-4**, N-(Phenoxycarbonyl)-L-valine 156732-13-7 156732-15-9 169597-13-1
RL: RCT (Reactant)

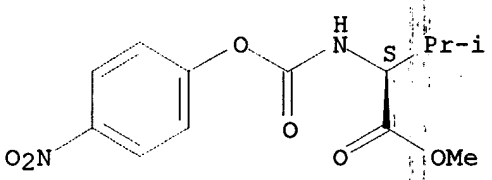
(starting material; pharmaceutical compn. of HIV protease inhibitor with improved oral bioavailability)

IT **162537-10-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(intermediate; pharmaceutical compn. of HIV protease inhibitor with improved oral bioavailability)

RN 162537-10-2 HCAPLUS

CN L-Valine, N-[(4-nitrophenoxy)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

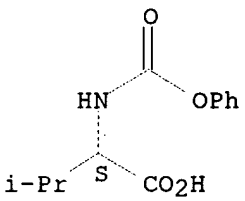


IT **126147-70-4**, N-(Phenoxycarbonyl)-L-valine
RL: RCT (Reactant)
(starting material; pharmaceutical compn. of HIV protease inhibitor with improved oral bioavailability)

RN 126147-70-4 HCAPLUS

CN L-Valine, N-(phenoxycarbonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L20 ANSWER 10 OF 12 HCAPLUS COPYRIGHT 2001 ACS

AN 1990:179761 HCAPLUS

DN 112:179761

TI Optical resolution of amino acid derivatives by high-performance liquid chromatography on tris(phenylcarbamate)s of cellulose and amylose

AU Okamoto, Yoshio; Kaida, Yuriko; Aburatani, Ryo; Hatada, Koichi

CS Fac. Eng. Sci., Osaka Univ., Toyonaka, 560, Japan

SO J. Chromatogr. (1989), 477(2), 367-76
CODEN: JOCRAM; ISSN: 0021-9673

DT Journal

LA English

CC 34-2 (**Amino Acids, Peptides,** and **Proteins**)

AB The optical resoln. of 10 N-protected alanine esters was examd. by **HPLC** using 6 cellulose and 5 amylose tris(phenylcarbamate) derivs. as chiral stationary phases. Tris(3,5-dimethylphenylcarbamate)s of both cellulose and amylose showed high resolving power for these racemates. The resoln. of 23 N-benzyloxycarbonyl .alpha.-amino acid ester was also tested on tris(3,5-dimethylphenylcarbamate)s of cellulose and amylose. All but 2 amino acid derivs. were completely resolved at least by one of the columns. On cellulose tris(3,5-dimethylphenylcarbamate), all L-amino

acids (except threonine) eluted first.

ST resoln amino ester **HPLC** cellulose trisphenylcarbamate; amylose trisphenylcarbamate resoln amino ester

IT Resolution
(of protected amino acid esters by **HPLC** on cellulose and amylose tris(phenylcabamate) stationary phases)

IT Chromatography, column and liquid
(high-performance, resoln. by, of protected amino acid esters with cellulose and amylose tris(phenylcarbmate) stationary phases)

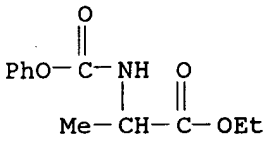
IT Amino acids, esters
RL: PROC (Process)
(N-protected, esters, resoln. of, by **HPLC** with cellulose and amylose tris(phenylcarbamate) stationary phases)

IT 4515-20-2 5143-72-6 5446-46-8, N-Benzoyl-DL-alanine ethyl ester 5513-39-3, N-Benzyloxycarbonyl-DL-alanine benzyl ester 5557-84-6 23161-27-5, N-Benzyloxycarbonyl-DL-serine ethyl ester 23161-28-6, N-Benzyloxycarbonyl-DL-threonine ethyl ester 25282-53-5, DL-Phenylalanine benzyl ester 39978-35-3, N-Benzyloxycarbonyl-DL-leucine ethyl ester 40489-45-0, N-Benzyloxycarbonyl-DL-serine benzyl ester 42998-42-5, N-Benzyloxycarbonyl-DL-valine ethyl ester 42998-44-7, N-Benzyloxycarbonyl-DL-phenylalanine ethyl ester 42998-45-8 46229-47-4, DL-Alanine benzyl ester 72604-32-1, N-tert-Butoxycarbonyl-DL-alanine ethyl ester 72604-33-2, N-Benzyloxycarbonyl-DL-alanine ethyl ester 85369-24-0 86827-19-2 **88406-41-1** 103063-37-2, N-Benzyloxycarbonyl-DL-phenylalanine benzyl ester 114285-13-1, N-Acetyl-DL-alanine benzyl ester 126400-85-9 126400-86-0 126400-87-1 126400-88-2 126400-89-3 126400-90-6 126400-91-7 126400-92-8 126400-93-9 126400-94-0, N-Benzoyl-DL-alanine benzyl ester 126400-95-1 **126400-96-2** 126400-97-3, N-Benzyloxycarbonyl-DL-valine benzyl ester 126400-98-4, N-Benzyloxycarbonyl-DL-norvaline ethyl ester 126400-99-5, N-Benzyloxycarbonyl-DL-norvaline benzyl ester 126401-00-1, N-Benzyloxycarbonyl-DL-leucine benzyl ester 126401-01-2, N-Benzyloxycarbonyl-DL-norleucine ethyl ester 126401-02-3, N-Benzyloxycarbonyl-DL-norleucine benzyl ester 126401-03-4, N-Benzyloxycarbonyl-DL-isoleucine benzyl ester 126401-04-5 126401-05-6 126401-06-7, N-Benzyloxycarbonyl-DL-threonine benzyl ester 126401-07-8 126401-08-9 126401-09-0 126401-10-3 126401-11-4 126401-12-5 126401-13-6 126401-14-7 126401-15-8 126401-16-9 126401-17-0 126401-18-1 126401-19-2 126401-20-5 126401-21-6, N-Benzyloxycarbonyl-DL-methionine benzyl ester 126401-22-7 126401-23-8 126433-60-1, N-Benzyloxycarbonyl-DL-methionine ethyl ester 126456-11-9 126456-12-0 126456-13-1, N-Benzyloxycarbonyl-DL-proline ethyl ester 126456-14-2, N-Benzyloxycarbonyl-DL-proline benzyl ester
RL: PROC (Process)
(resoln. of, by **HPLC** with cellulose and amylose tris(phenylcarbamate) stationary phases)

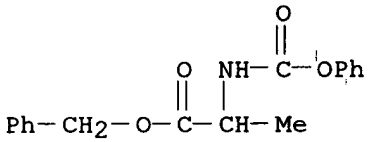
IT 9047-05-6, Amylose tris(phenylcarbamate) 9047-07-8, Cellulose tris(phenylcarbamate) 103938-40-5, Cellulose tris(4-bromophenylcarbamate) 103938-45-0, Cellulose tris(4-ethylphenylcarbamate) 103938-46-1, Cellulose tris(4-fluorophenylcarbamate) 103938-49-4 107028-63-7, Amylose tris(3,5-dichlorophenylcarbamate) 115901-94-5, Amylose tris(4-chlorophenylcarbamate) 115901-96-7, Amylose tris(4-methylphenylcarbamate)
RL: RCT (Reactant)
(stationary phase, for **HPLC** resoln. of protected alanine esters)

IT 103938-44-9, Cellulose tris(3,5-dimethylphenylcarbamate) 112049-40-8
RL: RCT (Reactant)
(stationary phase, for **HPLC** resoln. of protected amino acid

esters)
IT **88406-41-1 126400-96-2**
RL: PROC (Process)
(resoln. of, by **HPLC** with cellulose and amylose tris(phenylcarbamate) stationary phases)
RN 88406-41-1 HCAPLUS
CN Alanine, N-(phenoxycarbonyl)-, ethyl ester (9CI) (CA INDEX NAME)



RN 126400-96-2 HCAPLUS
CN Alanine, N-(phenoxycarbonyl)-, phenylmethyl ester (9CI) (CA INDEX NAME)



L20 ANSWER 11 OF 12 HCAPLUS COPYRIGHT 2001 ACS
AN 1988:611486 HCAPLUS
DN 109:211486
TI Preparation of heterocyclylpeptides as renin inhibitors
IN Ryono, Denis Evan; Weller, Harold Norris, III
PA Squibb, E. R., and Sons, Inc., USA
SO Eur. Pat. Appl., 143 pp.
CODEN: EPXXDW
DT Patent
LA English
IC ICM C07K005-06
ICS C07K005-08; C07D233-64; C07D417-12; C07D401-12; C07D403-12; A61K037-02; A61K037-64; A61K031-415; A61K031-425; A61K031-44
ICI C07D417-12, C07D277-00, C07D233-00; C07D401-12, C07D213-00, C07D233-00; C07D417-12, C07D235-00, C07D233-00
CC 34-3 (**Amino Acids, Peptides,** and **Proteins**)
Section cross-reference(s): 1
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 231919	A2	19870812	EP 1987-101373	19870202
EP 231919	A3	19900718		
EP 231919	B1	19930120		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
ZA 8700563	A	19870930	ZA 1987-563	19870126
AU 8768153	A1	19870806	AU 1987-68153	19870130
AU 595578	B2	19900405		
DK 8700523	A	19870804	DK 1987-523	19870202
HU 44576	A2	19880328	HU 1987-352	19870202
HU 203368	B	19910729		
AT 84793	E	19930215	AT 1987-101373	19870202

	ES 2043611	T3	19940101	ES 1987-101373	19870202
	JP 62258365	A2	19871110	JP 1987-23434	19870203
	CA 1310792	A1	19921124	CA 1987-528852	19870203
	US 4885292	A	19891205	US 1989-373633	19890629
PRAI	US 1986-825724		19860203		
	US 1987-3446		19870115		
	EP 1987-101373		19870202		

AB X-(NHCHR5CO)p-NHCHR4CONHCHR3CH(OH)R1 [I; X = R6(CH2)n, R6(CH2)nO2C, R6O(CH2)nCO, R6(CH2)nSO2, etc.; R1 = (substituted) N-contg. heterocyclyl; R3, R4, R5 = (halo)alkyl, arylalkyl, hydroxyalkyl, carboxyalkyl, guanidinoalkyl, imidazolylalkyl, etc.; R6 = alkyl, cycloalkyl, aryl, heterocyclyl; n = 0-5; p = 0, 1] useful as renin inhibitors, (no data) were prepd. N-[(1,1-Dimethylethoxy)carbonyl]-L-leucinal (prepn. from leucine given) in THF was added to a mixt. of BuLi and 1-[(phenylmethoxy)methyl]-1H-imidazole in THF at -70.degree.. The mixt. was kept at -70.degree. for 1 h, and at 0.degree. for 15 min followed by quenching with aq. NH4Cl and hydrolysis with HCl/EtOAc to give .alpha.-[(S)-1-amino-3-methylbutyl]-1-[(phenylmethoxy)methyl]-1H-imidazole-2-methanol-2HCl. The latter was coupled with N-[N-[(1,1-dimethylethoxy)carbonyl]-L-phenylalanyl]-1'-[phenylmethoxy)methyl]-L-histidine (prepn. given) using 1-hydroxybenzotriazole and DCC in DMF at ice temps. The coupling product was hydrogenolyzed in aq. MeOH contg. HCl over Pd/C to give N2-[N-[(1,1-dimethylethoxy)carbonyl]-L-phenylalanyl]-N-[(S)-1-[hydroxy(1H-imidazol-2-yl)methyl]-3-methylbutyl]-L-histidinamide-HOAc.

ST imidazolylpeptide prepn antihypertensive; Renin inhibitor peptide heterocyclyl; antihypertensive heterocyclylpeptide

IT Antihypertensives
(heterocyclyl-contg. peptide alcs.)

IT Peptides, preparation
RL: SPN (Synthetic preparation); PREP (Preparation)
(heterocyclyl-contg., prepn. of, as renin inhibitors)

IT 7693-46-1, 4-Nitrophenyl chloroformate
RL: RCT (Reactant)
(acylation by, of phenylalanine Me ester, in prepn. of antihypertensive)

IT 123-75-1, Pyrrolidine, reactions
RL: RCT (Reactant)
(acylation of, by phosgene, in prepn. of antihypertensive)

IT 100-39-0, Benzyl bromide
RL: RCT (Reactant)
(alkylation by, of di-Et benzylmalonate, in prepn. of antihypertensive)

IT 607-81-8, Diethyl benzylmalonate
RL: RCT (Reactant)
(alkylation of, by benzyl bromide)

IT 105-53-3, Diethyl malonate
RL: RCT (Reactant)
(alkylation of, by chloromethylnaphthalene, in prepn. of antihypertensive)

IT 6638-79-5, O,N-Dimethylhydroxylamine hydrochloride
RL: RCT (Reactant)
(amidation by, of (dimethylethoxycarbonylamino)cyclohexanepropanoic acid, in prepn. of antihypertensive)

IT 7524-50-7, L-Phenylalanine methyl ester hydrochloride
RL: RCT (Reactant)
(amidation by, of pyrrolidinecarbonyl chloride, in prepn. of antihypertensive)

IT 13139-15-6
RL: RCT (Reactant)
(amidation of, by dimethylhydroxylamine, in prepn. of antihypertensive)

IT 86-52-2, 1-Chloromethylnaphthalene
RL: RCT (Reactant)
(condensation of, with di-Et malonate, in prepn. of antihypertensive)
IT 61-90-5, L-Leucine, reactions
RL: RCT (Reactant)
(conversion of, to Et ester)
IT 71-00-1, L-Histidine, reactions
RL: PROC (Process)
(conversion of, to Me ester, in prepn. of antihypertensive)
IT 115888-02-3P
RL: SPN (Synthetic preparation); FORM (Formation, nonpreparative); PREP (Preparation)
(formation of, in prepn. of antihypertensive)
IT 288-47-1, Thiazole 49822-58-4
RL: RCT (Reactant)
(lithiation and condensation of, with leucinal deriv., in prepn. of antihypertensive)
IT 623-33-6, Glycine ethyl ester monohydrochloride 2666-93-5, L-Leucine methyl ester 13734-34-4 25024-53-7 25616-33-5 33014-68-5 83468-83-1 96867-10-6
RL: RCT (Reactant)
(peptide coupling of, in prepn. of antihypertensive)
IT 7389-87-9P, L-Histidine methyl ester dihydrochloride
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and N-protection of, in prepn. of antihypertensive)
IT 111629-38-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and coupling of, with phenylalanine deriv., in prepn. of antihypertensive)
IT 4372-32-1P 115766-40-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and decarboxylation of, in prepn. of antihypertensive)
IT 115766-26-2P 115766-27-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and deprotection of, in prepn. of antihypertensive)
IT 82010-31-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and oxidn. of, in prepn. of antihypertensive)
IT 115766-28-4P 115766-29-5P 115766-31-9P 115766-34-2P 115766-35-3P 115766-37-5P 115766-38-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and peptide coupling of, in prepn. of antihypertensive)
IT 7533-40-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and protection of, in prepn. of antihypertensive)
IT 20898-43-5P 111629-37-9P 115766-33-1P 115766-41-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, in prepn. of antihypertensive)
IT 2743-40-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and redn. of)
IT 51987-73-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and redn. of, in prepn. of antihypertensive)
IT 111629-39-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and sapon. of, in prepn. of antihypertensive)
IT 115765-65-6P 115765-66-7P 115765-67-8P 115765-68-9P 115765-69-0P 115765-70-3P 115765-71-4P 115765-72-5P 115765-73-6P 115765-74-7P 115765-76-9P 115765-77-0P 115765-78-1P 115765-79-2P 115765-80-5P

115765-81-6P 115765-82-7P 115765-83-8P 115765-84-9P 115765-86-1P
115765-88-3P 115766-42-2P 115766-43-3P 115802-91-0P 115887-98-4P
115888-03-4P 115888-04-5P 115888-05-6P 115888-06-7P 115888-07-8P
115888-08-9P 115888-09-0P 115888-86-3P 115935-94-9P 115935-95-0P
115935-96-1P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of, as antihypertensive)

IT 597-55-7P 618-68-8P 2481-59-6P 30189-51-6P 37736-82-6P
54601-21-7P 58521-45-2P 64152-76-7P 66605-57-0P
72155-45-4P 87694-50-6P 98105-42-1P 102639-04-3P 102639-05-4P
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115766-14-8P 115766-15-9P 115766-16-0P 115766-17-1P 115766-18-2P
115766-19-3P 115766-20-6P 115766-22-8P 115766-23-9P 115766-24-0P
115766-25-1P 115766-32-0P 115766-36-4P 115766-39-7P 115802-92-1P
115802-93-2P 115802-94-3P 115802-95-4P 115887-99-5P 115888-00-1P
115888-01-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for antihypertensive)

IT 115766-30-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediates for antihypertensive)

IT 1070-83-3, 3,3-Dimethylbutanoic acid
RL: RCT (Reactant)
(reaction of, in prepn. of antihypertensive peptide deriv.)

IT 109-01-3, 1-Methylpiperazine 110-91-8, Morpholine, reactions
RL: RCT (Reactant)
(reaction of, with (nitrophenoxycarbonyl)phenylalanine)

IT 70-34-8, 2,4-Dinitrofluorobenzene
RL: RCT (Reactant)
(reaction of, with histidine contg. dipeptide, in prepn. of antihypertensive)

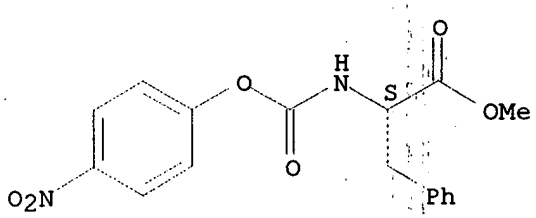
IT 68-11-1, Mercaptoacetic acid, uses and miscellaneous
RL: USES (Uses)
(**reagent**, for deprotection of dinitrophenylhistidine contg. peptide)

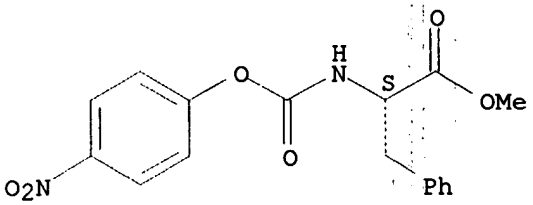
IT 3674-06-4
RL: RCT (Reactant)
(redn. of, in prepn. of antihypertensive)

IT **54601-21-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for antihypertensive)

RN 54601-21-7 HCAPLUS
CN L-Phenylalanine, N-[(4-nitrophenoxy)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.





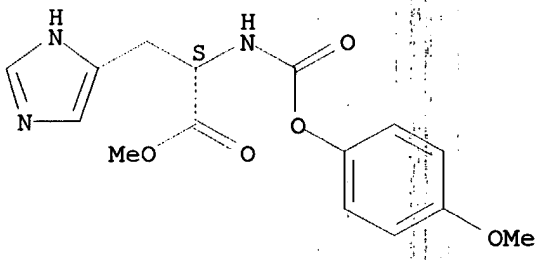
L20 ANSWER 12 OF 12 HCAPLUS COPYRIGHT 2001 ACS
AN 1974:437818 HCAPLUS
DN 81:37818
TI Histidine derivatives
PA Tanabe Seiyaku Co., Ltd.
SO Brit., 9 pp.
CODEN: BRXXAA
DT Patent
LA English
IC C07D; A61K
CC 34-3 (Synthesis of **Amino Acids, Peptides,** and **Proteins**)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI GB 1352414	A	19740508	GB 1971-12019	19710428

GI For diagram(s), see printed CA Issue.
AB L-Pyroglutamyl-L-proline amide (I), a thyrotropine-releasing or thyroid gland-stimulating factor, was prepd. from L-histidine Me ester (II). III-IV were prepd. from II by successive treatment with the appropriate chloride or azidoformate, hydrolysis, and tosylation. Condensation of these with L-proline amide at -10 to 10.degree. in the presence of a carbodiimide **reagent**, followed by treatment with N-benzyloxycarbonyl-L-pyroglutamic acid, and removal of the protecting groups, gave I.
ST histidine deriv
IT Protective groups
(alkoxycarbonyl and sulfenyl groups, for amino group of histidine methyl ester, in peptide prepn.)
IT Peptides, preparation
RL: PREP (Preparation)
(histidine- and proline-contg.)
IT (o-Nitrophenyl)sulfenyl group
(tert-Pentyloxy)carbonyl group
[(p-Methoxybenzyl)oxy]carbonyl group
tert-Butoxycarbonyl group
(protective group, for amino group in peptide prepn.)
IT Amino group
(protective groups for, alkoxycarbonyl and sulfenyl groups as, in peptide prepn.)
IT Imido group
(protective groups for, benzyl and tert-akyloxycarbonyl groups as, in peptide prepn.)
IT (Benzyloxy)carbonyl group
(protective groups, for imido group in peptide prepn.)
IT 7531-52-4
RL: RCT (Reactant)
(condensation of, with histidines)
IT 15354-08-2P 23241-50-1P 23241-51-2P 24305-27-9P 35899-43-5P
35899-44-6P 35899-45-7P 35899-46-8P 35899-47-9P 35899-49-1P

53090-17-8P 53090-19-0P 53090-21-4P 53090-24-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
IT 98-79-3
RL: RCT (Reactant)
(protective group for imido group of, in peptide prepn.)
IT 7389-87-9
RL: RCT (Reactant)
(protective groups for .alpha.-amino group of, in peptide prepn.)
IT 5591-72-0 7669-54-7 24608-52-4 40438-33-3
RL: RCT (Reactant)
(reaction of, with histidine methyl ester)
IT 32159-21-0 53090-23-6
RL: RCT (Reactant)
(reaction of, with histidyl prolinamide)
IT **53090-17-8P 53090-19-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 53090-17-8 HCAPLUS
CN L-Histidine, N-[(4-methoxyphenoxy)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

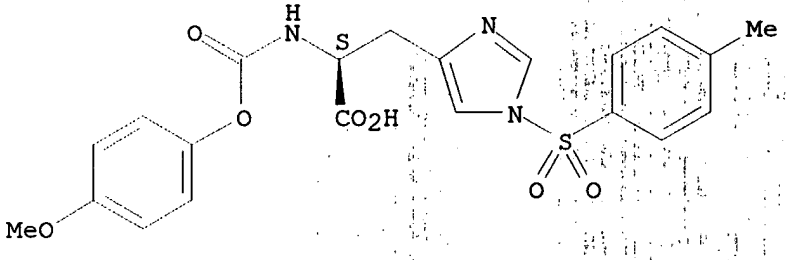


RN 53090-19-0 HCAPLUS
CN L-Histidine, N-[(4-methoxyphenoxy)carbonyl]-1-[(4-methylphenyl)sulfonyl]-, compd. with N-cyclohexylcyclohexanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

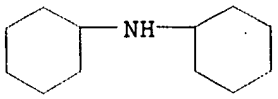
CRN 53090-18-9
CMF C21 H21 N3 O7 S
CDES 5:L

Absolute stereochemistry.

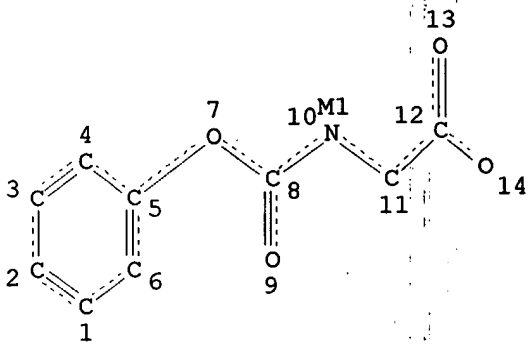


CM 2

CRN 101-83-7
CMF C12 H23 N



L1 STR

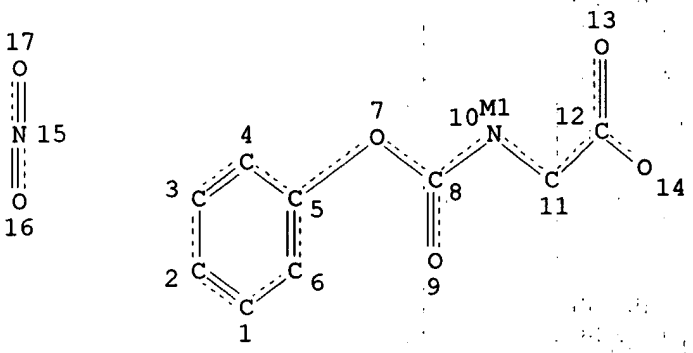


NODE ATTRIBUTES:
HCOUNT IS M1 AT 10
NSPEC IS R AT 1
NSPEC IS R AT 2
NSPEC IS R AT 3
NSPEC IS R AT 4
NSPEC IS R AT 5
NSPEC IS R AT 6
NSPEC IS C AT 7
NSPEC IS C AT 8
NSPEC IS C AT 9
NSPEC IS C AT 10
NSPEC IS C AT 11
NSPEC IS C AT 12
NSPEC IS C AT 13
NSPEC IS C AT 14
DEFAULT MLEVEL IS ATOM
MLEVEL IS CLASS AT 7 8 9 10 11 12 13 14
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 14

STEREO ATTRIBUTES: NONE

L3	501	SEA FILE=REGISTRY SSS FUL L1
L4	213	SEA FILE=HCAPLUS ABB=ON PLU=ON L3
L6	1	SEA FILE=HCAPLUS ABB=ON PLU=ON 2000:755247/AN
L14	75483	SEA FILE=HCAPLUS ABB=ON PLU=ON (AMINO ACIDS OR PEPTIDES OR PROTEINS)/CC
L15	83	SEA FILE=HCAPLUS ABB=ON PLU=ON L4 AND L14
L16	82	SEA FILE=HCAPLUS ABB=ON PLU=ON L15 NOT L6
L18	4	SEA FILE=HCAPLUS ABB=ON PLU=ON (HPLC OR CHROMATOGARPH?) AND L16
L19	9	SEA FILE=HCAPLUS ABB=ON PLU=ON (ENANTIO? OR SEPARAT? OR CHROMOPHO? OR REAGENT) AND L16
L20	12	SEA FILE=HCAPLUS ABB=ON PLU=ON L18 OR L19
L21		STR



NODE ATTRIBUTES:
HCOUNT IS M1 AT 10
NSPEC IS R AT 1
NSPEC IS R AT 2
NSPEC IS R AT 3
NSPEC IS R AT 4
NSPEC IS R AT 5
NSPEC IS R AT 6
NSPEC IS C AT 7
NSPEC IS C AT 8
NSPEC IS C AT 9
NSPEC IS C AT 10
NSPEC IS C AT 11
NSPEC IS C AT 12
NSPEC IS C AT 13
NSPEC IS C AT 14
NSPEC IS C AT 15
NSPEC IS C AT 16
NSPEC IS C AT 17
DEFAULT MLEVEL IS ATOM
MLEVEL IS CLASS AT 7 8 9 10 11 12 13 14 15 16 17
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 17

STEREO ATTRIBUTES: NONE
L23 87 SEA FILE=REGISTRY SUB=L3 SSS FUL L21
L24 56 SEA FILE=HCAPLUS ABB=ON PLU=ON L23
L25 50 SEA FILE=HCAPLUS ABB=ON PLU=ON L24 NOT L20
L26 49 SEA FILE=HCAPLUS ABB=ON PLU=ON L25 NOT L6
L27 24 SEA FILE=HCAPLUS ABB=ON PLU=ON L14 AND L26

L27 ANSWER 1 OF 24 HCAPLUS COPYRIGHT 2001 ACS
AN 2001:416903 HCAPLUS
DN 135:33643
TI Preparation of 3-(2-aminoethylthio)methyl-4-oxo-4-(3-pyridyl)butanoic acid derivatives as neuroprotective agents
IN Bhagwat, Shripad; Palanki, Moorthy; Erdman, Paul; Doubleday, Mary; Sato, Hiroshi
PA Nippon Kayaku Co., Ltd., Japan
SO PCT Int. Appl., 119 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D213-55
ICS C07D213-56; C07D417-12; A61K031-44; A61P025-00
CC 34-2 (**Amino Acids, Peptides,** and **Proteins**)
Section cross-reference(s): 1, 27
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001040187	A2	20010607	WO 2000-JP8090	20001116

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 1999-450245 A 19991129
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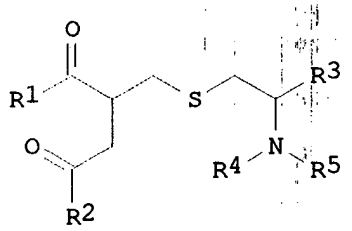

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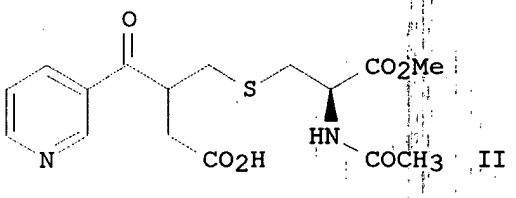

II

AB The title compds. [I; R1 = (un)substituted alkyl, aryl, arylakyl, etc.; R2 = OR2a, NR2bR2c; R3 = H, :O, CO2R3a, etc.; R4 = H, (un)substituted alkyl, aryl, etc.; R3 and R4 taken together = (un)substituted heterocyclyl; R5 = H, (un)substituted alkyl; R2a = H, (un)substituted alkyl, aryl, etc.; R2b, R2c = H, (un)substituted alkyl, aryl, etc.; NR2bR2c = (un)substituted heterocyclyl; R3a = H, (un)substituted alkyl, aryl, etc.] which have

utility in the treatment of conditions which benefit from administration of neuroprotective agents generally, including treatment of central and peripheral nervous condition as well as for promoting nerve cell differentiation, were prepd. Thus, reacting 4-oxo-3-(piperidylmethyl)-4-(3-pyridyl)butanoic acid with Me N-acetyl-L-cysteine ester in EtOH afforded 85% (R)-II. Biol. data for compds. I were given.

ST aminoethylthiomethyloxopyridylbutanoic acid prepn neuroprotectant; pyridylbutanoic acid aminoethylthiomethyloxo prepn neuroprotectant

IT Cytoprotective agents
(neuroprotectants; prepn. of 3-(2-aminoethylthio)methyl-4-oxo-4-(3-pyridyl)butanoic acid derivs. as neuroprotective agents)

IT 343574-29-8P 343574-71-0P 343575-87-1P 343575-92-8P 343577-16-2P
343577-17-3P 343577-23-1P 343577-91-3P
RL: BAC (Biological activity or effector, except adverse); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 3-(2-aminoethylthio)methyl-4-oxo-4-(3-pyridyl)butanoic acid derivs. as neuroprotective agents)

IT 220301-04-2P 343573-75-1P 343573-76-2P 343573-77-3P 343573-78-4P
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343576-09-0P 343576-10-3P 343576-11-4P 343576-12-5P 343576-13-6P
343576-14-7P 343576-15-8P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 3-(2-aminoethylthio)methyl-4-oxo-4-(3-pyridyl)butanoic acid derivs. as neuroprotective agents)

IT 343576-16-9P 343576-17-0P 343576-18-1P 343576-19-2P 343576-20-5P
343576-21-6P 343576-22-7P 343576-23-8P 343576-24-9P 343576-25-0P
343576-26-1P 343576-27-2P 343576-28-3P 343576-29-4P 343576-30-7P
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RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 3-(2-aminoethylthio)methyl-4-oxo-4-(3-pyridyl)butanoic acid derivs. as neuroprotective agents)

IT 71-23-8, n-Propanol, reactions 86-84-0, 1-Naphthyl isocyanate 96-33-3, Methyl acrylate 104-12-1, 4-Chlorophenyl isocyanate 104-97-2,

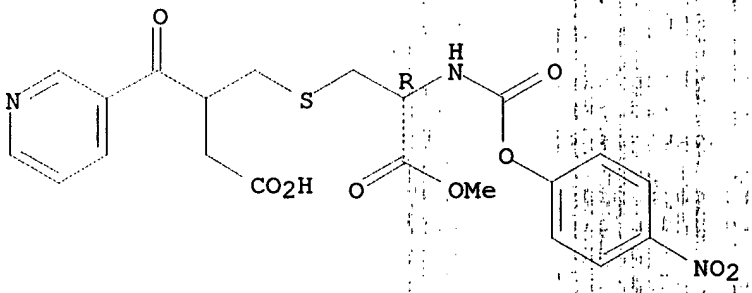
Cyclopentanepropanoyl chloride 110-89-4, Piperidine, reactions 140-88-5, Ethyl acrylate 141-32-2 500-22-1, 3-Pyridinecarboxaldehyde 501-53-1, Benzyl chloroformate 622-58-2, 4-Methylphenyl isocyanate 700-87-8, 2-Methoxyphenyl isocyanate 1016-19-9, 3,4,5-Trimethoxyphenyl isocyanate 1190-73-4, n-Acetylcysteamine 1195-45-5, 4-Fluorophenyl isocyanate 1476-23-9, Allyl isocyanate 2859-67-8, 3-Pyridinepropanol 3025-95-4 3173-53-3, Cyclohexyl isocyanate 4192-31-8, 4-Oxo-4-(3-pyridyl)butanoic acid 4530-20-5 6068-72-0, 4-Cyanobenzoyl chloride 7652-46-2 15159-40-7, Morpholine-4-carbonyl chloride 16744-98-2, 2-Fluorophenyl isocyanate 20938-74-3 36643-74-0, Indanol 54132-75-1, 3,5-Dimethylphenyl isocyanate 59587-09-6 67385-09-5 69812-29-9 129714-97-2, 3,5-Difluorobenzoyl chloride 220301-12-2 343578-28-9 343578-29-0 343578-30-3
RL: RCT (Reactant)
(prepn. of 3-(2-aminoethylthio)methyl-4-oxo-4-(3-pyridyl)butanoic acid derivs. as neuroprotective agents)

IT 59086-27-0P 61192-47-0P 343573-70-6P 343573-71-7P 343573-72-8P 343578-26-7P 343578-27-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of 3-(2-aminoethylthio)methyl-4-oxo-4-(3-pyridyl)butanoic acid derivs. as neuroprotective agents)

IT **343575-47-3P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 3-(2-aminoethylthio)methyl-4-oxo-4-(3-pyridyl)butanoic acid derivs. as neuroprotective agents)

RN 343575-47-3 HCAPLUS
CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.



L27 ANSWER 2 OF 24 HCAPLUS COPYRIGHT 2001 ACS
AN 2000:592548 HCAPLUS
DN 133:177486
TI Preparation of substituted stilbene compounds with vascular damaging activity
IN Davis, Peter David
PA Angiogene Pharmaceuticals Ltd., UK
SO PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-195
ICS A61P035-00; A61P017-00; A61P027-02
CC 34-2 (**Amino Acids, Peptides,** and **Proteins**)

Section cross-reference(s): 1, 25

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000048590	A1	20000824	WO 2000-GB503	20000215

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI GB 1999-3403 A 19990216

OS MARPAT 133:177486

AB A vascular damaging agent AXB (A = substituted cis-stilbene; X = linker bond, atom, or group; B = moiety derived from an inhibitor of the formation or action of NO in mammalian systems), is claimed. Thus, (Z)-1-[3-(N-.alpha.-tert-butoxycarbonyl-N-.omega.-nitroarginyloxy)-4-methoxyphenyl]-2-(3,4,5-trimethoxyphenyl)ethene was stirred with CF3CO2H in CH2Cl2 to give (Z)-1-(4-methoxy-3-NG-nitroarginyloxyphenyl)-2-(3,4,5-trimethoxyphenyl)ethene. The latter at 50 mg/kg i.p. in mice bearing CaNT or SaS tumors gave 95% redn. in vascular vol. and 91-100% tumor necrosis.

ST vascular damaging agent substituted stilbene prepn; neovascularization disease treatment substituted stilbene; nitroarginyloxystilbene prepn tumor vascular damaging activity; nitric oxide synthase inhibitor nitroarginyloxystilbene prepn

IT Angiogenesis
(neovascularization, treatment of diseases involving neovascularization; prepn. of substituted stilbene compds. with vascular damaging activity)

IT Amino acids, preparation
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(nitroarginyloxystilbene derivs.; prepn. of substituted stilbene compds. with vascular damaging activity)

IT Antitumor agents
(prepn. of substituted stilbene compds. with vascular damaging activity)

IT 125978-95-2, Nitric oxide synthase
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(inhibitors; prepn. of substituted stilbene compds. with vascular damaging activity)

IT 288585-54-6P **288585-55-7P 288585-56-8P 288585-57-9P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of substituted stilbene compds. with vascular damaging activity)

IT 51298-62-5 61240-20-8, 3,4,5-Trimethoxybenzyltriphenylphosphonium bromide 97315-18-9 117048-59-6 288585-58-0
RL: RCT (Reactant)
(prepn. of substituted stilbene compds. with vascular damaging activity)

IT 288585-59-1P 288585-60-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)

(prepn. of substituted stilbene compds. with vascular damaging activity)

RE.CNT 5

RE

(1) Ajinomoto Kk; EP 0641767 A 1995 HCAPLUS

(2) Aston Molecules Ltd; WO 9216486 A 1992 HCAPLUS

(3) George, R; ANTI-CANCER DRUG DESIGN 1995, V10(4), P299

(4) Koji, O; JOURNAL OF MEDICINAL CHEMISTRY 1998, V41(16), P3022

(5) Ohsumi, K; BIOORGANIC & MEDICINAL CHEMISTRY LETTERS 1998, V8(22), P3153 HCAPLUS

IT **288585-55-7P 288585-56-8P 288585-57-9P**

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

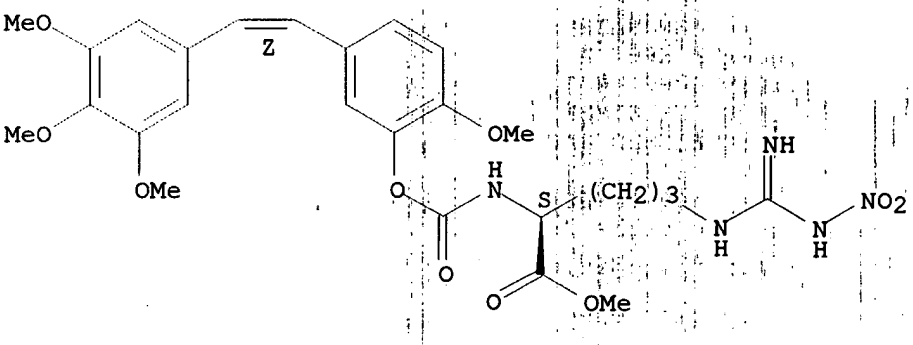
(prepn. of substituted stilbene compds. with vascular damaging activity)

RN 288585-55-7 HCAPLUS

CN L-Ornithine, N5-[imino(nitroamino)methyl]-N2-[[2-methoxy-5-[(1Z)-2-(3,4,5-trimethoxyphenyl)ethenyl]phenoxy]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

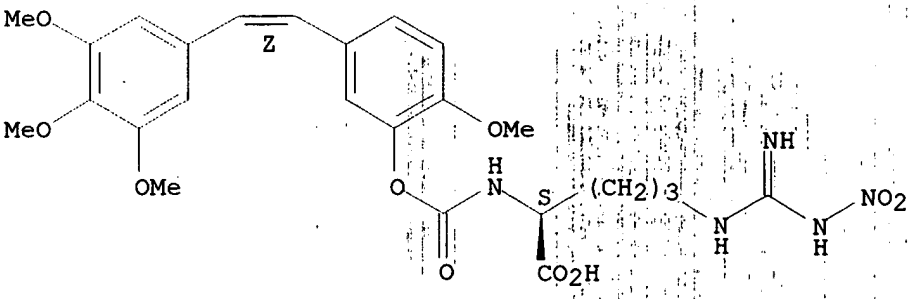


RN 288585-56-8 HCAPLUS

CN L-Ornithine, N5-[imino(nitroamino)methyl]-N2-[[2-methoxy-5-[(1Z)-2-(3,4,5-trimethoxyphenyl)ethenyl]phenoxy]carbonyl]-, (9CI) (CA INDEX NAME)

Absolute stereochemistry.

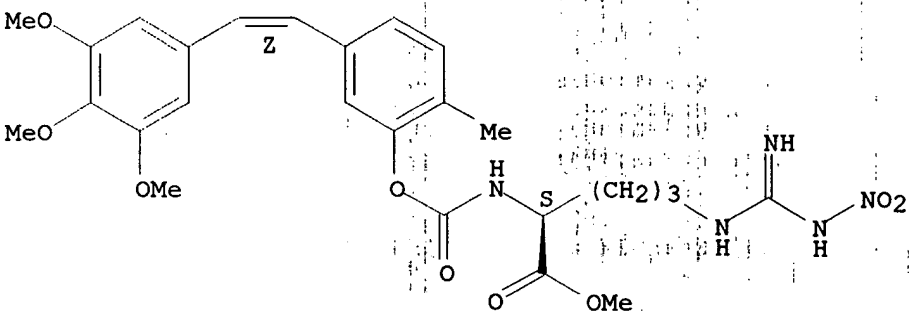
Double bond geometry as shown.



RN 288585-57-9 HCAPLUS

CN L-Ornithine, N5-[imino(nitroamino)methyl]-N2-[[2-methyl-5-[(1Z)-2-(3,4,5-trimethoxyphenyl)ethenyl]phenoxy]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L27 ANSWER 3 OF 24 HCAPLUS COPYRIGHT 2001 ACS
AN 1999:753019 HCAPLUS
DN 132:12506
TI Preparation of peptides for treating diseases of excessive bone loss or cartilage or matrix degradation as cysteine protease inhibitors
IN Bondinell, William Edward; Desjarlais, Renee Louise; Veber, Daniel Frank; Yamashita, Dennis Shinji
PA Smithkline Beecham Corporation, USA
SO PCT Int. Appl., 128 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K
CC 34-3 (**Amino Acids, Peptides,** and **Proteins**)
Section cross-reference(s): 1, 7, 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9959526	A2	19991125	WO 1999-US11266	19990520
	WO 9959526	A3	20000120		
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	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1067894	A2	20010117	EP 1999-924421	19990520
	R: BE, CH, DE, ES, FR, GB, IT, LI, NL				
PRAI	US 1998-86557	P	19980521		
	WO 1999-US11266	W	19990520		

OS MARPAT 132:12506
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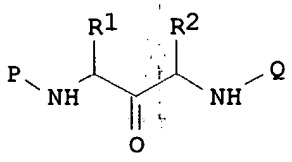

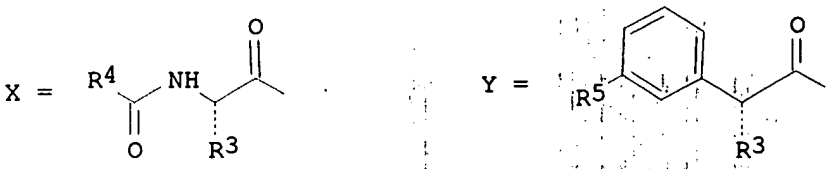

AB The present invention provides peptides bis-aminomethyl carbonyl protease inhibitors I (R1, R2 = alkyl; P = X, Y; R3 selected from the group consisting of: CH2CH(CH3)2, CH2CH2CH3, CH2CH=CH2, or CH2Ph; R4 is selected from the group consisting of alkyl; N-piperazine; N-tetrahydroisoquinoline; substituted alkyl, Ph, benzofuran, benzothiazole; quinoline; naphthyl; and benzoxazole; R5 = Ph and Ph substituted with alkyl, N-piperidine, benzofuran; pyridine; Q = arylacyl) and pharmaceutically acceptable salts, hydrates and solvates thereof which inhibit proteases, including cathepsin K, pharmaceutical compns. of such compds., and methods for treating diseases of excessive bone loss or cartilage or matrix degrdn., including osteoporosis; gingival disease including gingivitis and periodontitis; arthritis, more specifically, osteoarthritis and rheumatoid arthritis; Paget's disease; hypercalcemia of malignancy; and metabolic bone disease, comprising inhibiting said bone loss or excessive cartilage or matrix degrdn. by administering to a patient in need thereof a compd. of the present invention. Thus, (S)-3N-(N-(thianaphthenyl-2-carbonyl)-leucinyl)-amino-1N-(3-{2-(1-oxo)-pyridyl}phenylacetyl)-amino-butan-2-one was prepd. for treating diseases of excessive bone loss or cartilage or matrix degrdn. as cysteine protease inhibitor. Detn. of cathepsin K proteolytic catalytic activity of these compds. are reported.

ST osteoarthritis osteoporosis rheumatoid arthritis peptide prepn; bone loss cartilage degrdn peptide prepn protease inhibitor

IT Cartilage
(degeneration; prepn. of peptides for treating diseases of excessive bone loss or cartilage or matrix degrdn. as cysteine protease inhibitors)

IT Bone
(demineralization; prepn. of peptides for treating diseases of excessive bone loss or cartilage or matrix degrdn. as cysteine protease inhibitors)

IT Bone, disease
Osteoarthritis
Osteoporosis
Rheumatoid arthritis
(prepn. of peptides for treating diseases of excessive bone loss or cartilage or matrix degrdn. as cysteine protease inhibitors)

IT Peptides, preparation
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of peptides for treating diseases of excessive bone loss or cartilage or matrix degrdn. as cysteine protease inhibitors)

IT 251458-51-2P
RL: BAC (Biological activity or effector, except adverse); RCT (Reactant);

SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of peptides for treating diseases of excessive bone loss or cartilage or matrix degrdn. as cysteine protease inhibitors)

IT 247119-79-5P 247119-80-8P 247119-82-0P 247119-83-1P 251457-08-6P
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251458-69-2P 251458-70-5P 251458-71-6P 251458-78-3P 251458-79-4P
251458-80-7P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of peptides for treating diseases of excessive bone loss or cartilage or matrix degrdn. as cysteine protease inhibitors)

IT 37353-41-6, Cysteine protease
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(prepn. of peptides for treating diseases of excessive bone loss or cartilage or matrix degrdn. as cysteine protease inhibitors)

IT 50-43-1, 2,4,6-Trichlorobenzoic acid 51-44-5, 3,4-Dichlorobenzoic acid 65-85-0, Benzoic acid, reactions 75-08-1, Ethanethiol 79-09-4, Propionic acid, reactions 86-59-9, 8-Quinoline-carboxylic acid 88-13-1, Thiophene-3-carboxylic acid 91-21-4, 1,2,3,4-Tetrahydroisoquinoline 92-92-2, Biphenyl-4-carboxylic acid" 93-07-2, 3,4-Dimethoxybenzoic acid" 93-09-4, 2-Naphthoicacid 93-10-7, 2-Quinolinylcarboxylic acid 98-09-9, Benzenesulfonyl chloride 98-97-5, Pyrazine-2-carboxylic acid" 99-96-7, 4-Hydroxybenzoic acid, reactions 100-00-5, 1-Chloro-4-nitro-benzene 100-09-4, 4-Methoxybenzoic acid" 109-01-3 109-52-4, Valeric acid, reactions 142-25-6 349-88-2, 4-Fluorophenylsulfonyl chloride 371-40-4, 4-Fluoro-aniline 402-54-0 455-24-3, 4-(Trifluoromethyl)benzoic acid 456-22-4, 4-Fluoro-benzoic acid 496-41-3, Benzofuran-2-carboxylic acid 501-52-0, 3-Phenylpropionic acid 504-29-0, 2-Amino-pyridine 536-69-6, 5-Butylpyridine-2-carboxylic acid 585-76-2, 3-Bromo-benzoic acid 611-95-0, 4-(Benzoyl)benzoic acid 616-29-5, 1,3-Diamino-propan-2-ol 619-45-4, 4-Methoxycarbonyl-aniline 620-86-0 622-40-2, 4-(2-Hydroxyethyl)morpholine 636-82-8, 1-Cyclohexene-1-carboxylic acid 646-07-1 661-69-8, Hexamethylditin 828-51-3, Adamantane-1-carboxylic acid 883-21-6, 1-Methoxy-2-naphthoicacid 883-62-5, 3-Methoxy-2-naphthoic acid 1457-59-6, 5-Methylimidazolyl-4-carboxylic acid 1477-50-5, Indole-2-carboxylic acid 1486-51-7 1623-92-3,

4-Phenoxybenzenesulfonyl chloride 1670-82-2, Indole-6-carboxylic acid 1723-27-9, Thieno[3,2-b]thiophene-2-carboxylic acid 1878-67-7, 3-Bromo phenyl acetic acid 2008-75-5, 2-(Piperidin-1-yl)ethyl chloride hydrochloride" 2666-93-5 2991-42-6, 4-Trifluoromethylbenzenesulfonyl chloride 3328-70-9, 5-Formylsalicylaldehyde 3510-66-5, 2-Bromo-5-methylpyridine 3622-35-3, 6-Benzothiazolecarboxylic acid 3647-69-6, 2-(4-Morpholinyl)ethyl chloride hydrochloride 4457-32-3, 4-Nitrobenzyl chloroformate 4467-07-6, 3-(2-Pyridyl)benzoic acid 4926-28-7, 2-Bromo-4-methylpyridine 5315-25-3, 2-Bromo-6-methylpyridine 5731-13-5 6314-28-9, Benzo[b]thiophene-2-carboxylic acid 6315-89-5, 3,4-Dimethoxy-aniline 6480-68-8, 3-Quinolinecarboxylic acid 6702-50-7, Methyl 3-hydroxy-4-methoxy-benzoate 6973-60-0 7250-53-5, 5-Quinoline-carboxylic acid 10147-37-2, Isopropyl sulfonyl chloride 10349-57-2, 6-Quinolinecarboxylic acid 15112-41-1, 5-Benzoxazolecarboxylic acid 16309-45-8 16419-60-6 19438-10-9, Methyl 3-hydroxybenzoate 20029-52-1, 4-Cyclohexylbenzoic acid 27298-97-1 31462-59-6, Pyrimidine-4-carboxylic acid 32315-10-9, Triphosgene 40274-67-7 50551-56-9 50793-29-8, 4-(4-Cyanophenoxy)benzoic acid 57260-71-6, 1-(tert-Butoxycarbonyl)piperazine 65007-00-3 66715-65-9, 2-Pyridinesulfonyl chloride 68947-43-3, N-Methylpiperidine-4-carboxylic acid 73579-08-5 78161-82-7, 4-(4-(Trifluoromethyl)phenoxy)benzoic acid 81432-12-4 90433-20-8 92198-45-3 98327-87-8, 2,2'-Bis(diphenylphosphino)-1,1'-binaphthyl 98437-24-2, 2-Benzofuran boronic acid 144059-86-9 150529-73-0, Methyl 3-bromophenylacetate 150798-78-0 154235-77-5, Benzoxazole-6-carboxylic acid 154739-53-4 175137-58-3 175201-51-1 190661-70-2 210304-58-8 215947-98-1 228419-12-3 248923-01-5 251457-20-2 251457-33-7 **251457-72-4** 251457-88-2 251458-03-4 251458-15-8 251458-26-1 251458-30-7 251458-34-1 251458-38-5 251458-39-6 251458-73-8

RL: RCT (Reactant)

(prepn. of peptides for treating diseases of excessive bone loss or cartilage or matrix degrdn. as cysteine protease inhibitors)

IT 23948-77-8P, [1,1'-Biphenyl]-3-acetic acid 51061-68-8P 69038-74-0P 75852-28-7P 99370-68-0P 203503-06-4P 215309-01-6P 216316-23-3P 216316-24-4P 216316-27-7P 224643-30-5P 227178-31-6P 227178-32-7P 229630-60-8P 247119-96-6P 247119-99-9P 247122-09-4P 250726-45-5P 250726-46-6P 250726-47-7P 251457-05-3P 251457-06-4P 251457-07-5P 251457-11-1P 251457-12-2P 251457-13-3P 251457-22-4P 251457-25-7P 251457-26-8P 251457-29-1P 251457-31-5P 251457-57-5P 251457-58-6P 251457-59-7P 251457-61-1P 251457-63-3P 251457-67-7P 251457-70-2P 251457-73-5P 251458-00-1P 251458-07-8P 251458-14-7P 251458-16-9P 251458-21-6P 251458-22-7P 251458-23-8P 251458-25-0P 251458-27-2P 251458-28-3P 251458-36-3P 251458-46-5P 251458-47-6P 251458-48-7P 251458-49-8P 251458-72-7P 251458-74-9P 251458-75-0P 251458-76-1P 251458-77-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)

(prepn. of peptides for treating diseases of excessive bone loss or cartilage or matrix degrdn. as cysteine protease inhibitors)

IT **251457-72-4**

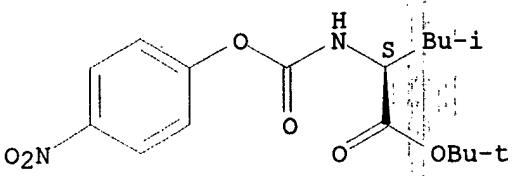
RL: RCT (Reactant)

(prepn. of peptides for treating diseases of excessive bone loss or cartilage or matrix degrdn. as cysteine protease inhibitors)

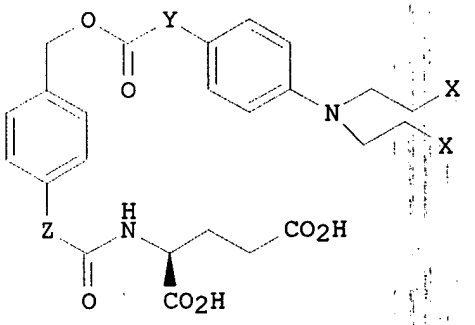
RN 251457-72-4 HCAPLUS

CN L-Leucine, N-[(4-nitrophenoxy)carbonyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L27 ANSWER 4 OF 24 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:749736 HCAPLUS
DN 130:110572
TI Self-Immolative Nitrogen Mustard Prodrugs for Suicide Gene Therapy
AU Niculescu-Duvaz, Dan; Niculescu-Duvaz, Ion; Friedlos, Frank; Martin, Janet; Spooner, Robert; Davies, Lawrence; Marais, Richard; Springer, Caroline J.
CS UK
SO J. Med. Chem. (1998), 41(26), 5297-5309
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
CC 34-2 (**Amino Acids, Peptides,** and **Proteins**)
Section cross-reference(s): 1, 25
GI



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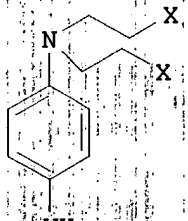
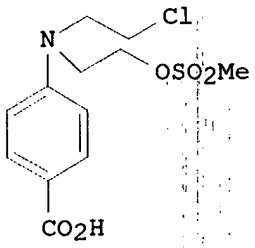


II



III

AB Four new potential self-immolative prodrugs derived from phenol and aniline nitrogen mustards, four model compds. derived from their corresponding fluoroethyl analogs and two new self-immolative linkers were designed and synthesized for use in the suicide gene therapy termed GDEPT (gene-directed enzyme prodrug therapy). The self-immolative prodrugs were designed to be activated by the enzyme carboxypeptidase G2 (CPG2) releasing an active drug by a 1,6-elimination mechanism via an unstable intermediate. Thus, glutamate derivs. I (Y = O, NH; Y = O, NH; X = Cl)

were synthesized. They are bifunctional alkylating agents in which the activating effects of the phenolic hydroxyl or amino functions are masked through an oxycarbonyl or a carbamoyl bond to a benzylic spacer which is itself linked to a glutamic acid by an oxycarbonyl or a carbamoyl bond. The corresponding fluoroethyl compds. I (X = F) were also synthesized. The rationale was to obtain model compds. with greatly reduced alkylating abilities that would be much less reactive with nucleophiles compared to the corresponding chloroethyl derivs. This enabled studies of these model compds. as substrates for CPG2, without incurring the rapid and complicated decompn. pathways of the chloroethyl derivs. The prodrugs were designed to be activated to their corresponding phenol and aniline nitrogen mustard drugs by CPG2 for use in GDEPT. The synthesis of the analogous novel parent drugs II is also described. A colorectal cell line was engineered to express CPG2 tethered to the outer cell surface. The phenylenediamine compds. were found to behave as prodrugs, yielding IC50 prodrug/IC50 drug ratios between 20- and 33-fold for I (X = Cl, Y = NH; Z = O, NH) and differentials of 12-14-fold between CPG2-expressing and control LacZ-expressing clones. The drugs released are up to 70-fold more potent than benzoic acid III that results from the glutamate prodrug (CMDA) which has been used previously for GDEPT. These data demonstrate the viability of this strategy and indicate that self-immolative prodrugs can be synthesized to release potent mustard drugs selectively by cells expressing CPG2 tethered to the cell surface in GDEPT.

ST glutamate nitrogen mustard prodrug prepn suicide gene therapy; immolative nitrogen mustard prodrug suicide gene therapy; carboxypeptidase G2 cleavage glutamate nitrogen mustard prodrug prepn; anticancer agent glutamate nitrogen mustard prodrug prepn; cytotoxicity glutamate nitrogen mustard prodrug prepn

IT Chemotherapy
(gene-directed enzyme prodrug; prepn. of self-immolative nitrogen mustard prodrugs for suicide gene therapy)

IT Antitumor agents
Cytotoxicity
Gene therapy
Prodrugs
(prepn. of self-immolative nitrogen mustard prodrugs for suicide gene therapy)

IT 122665-70-7
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(prepn. of self-immolative nitrogen mustard prodrugs for suicide gene therapy)

IT 1204-69-9, 4-[Bis(2-chloroethyl)amino]phenol 2067-58-5
RL: BAC (Biological activity or effector, except adverse); RCT (Reactant); BIOL (Biological study)
(prepn. of self-immolative nitrogen mustard prodrugs for suicide gene therapy)

IT 219591-87-4P 219592-00-4P
RL: BAC (Biological activity or effector, except adverse); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of self-immolative nitrogen mustard prodrugs for suicide gene therapy)

IT 122665-73-0DP, N-4-[(2-Chloroethyl)(2-mesyloxyethyl)amino]benzoyl-L-glutamic acid, dichloro and difluoro carbonate and carbamate analogs
180838-98-6P 180839-01-4P 180839-03-6P 180839-05-8P 219591-76-1P
219591-80-7P 219591-82-9P 219591-86-3P 219591-92-1P 219591-94-3P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of self-immolative nitrogen mustard prodrugs for suicide gene therapy)

IT 9074-87-7, Carboxypeptidase G2
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(prepn. of self-immolative nitrogen mustard prodrugs for suicide gene therapy)
IT 219591-77-2P 219591-79-4P
RL: BYP (Byproduct); PREP (Preparation)
(prepn. of self-immolative nitrogen mustard prodrugs for suicide gene therapy)
IT 219591-73-8P
RL: BYP (Byproduct); RCT (Reactant); PREP (Preparation)
(prepn. of self-immolative nitrogen mustard prodrugs for suicide gene therapy)
IT 123-08-0, 4-Hydroxybenzaldehyde 619-73-8, 4-Nitrobenzyl alcohol
18226-17-0 20845-16-3 32677-01-3, Di-tert-butyl L-glutamate hydrochloride 101582-69-8
RL: RCT (Reactant)
(prepn. of self-immolative nitrogen mustard prodrugs for suicide gene therapy)
IT 18483-99-3P 18484-05-4P 57529-05-2P 113068-95-4P 161803-03-8P
161803-04-9P 161803-05-0P 161803-06-1P 180838-97-5P 180839-00-3P
180839-02-5P 180839-04-7P 180839-06-9P 180839-11-6P 180839-13-8P
180839-14-9P 180839-15-0P 180839-16-1P 180839-18-3P 180839-19-4P
180839-20-7P 180839-21-8P 180841-62-7P 219591-81-8P
219591-83-0P 219591-85-2P 219591-91-0P 219591-93-2P 219591-96-5P
219591-97-6P 219591-98-7P 219592-01-5P 219592-02-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of self-immolative nitrogen mustard prodrugs for suicide gene therapy)
IT 219591-75-0P 219591-89-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of self-immolative nitrogen mustard prodrugs for suicide gene therapy)
RE.CNT 29
RE

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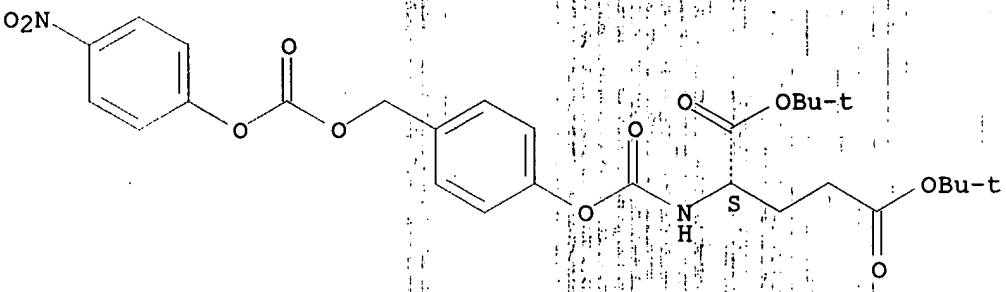
IT **180839-20-7P 180839-21-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of self-immolative nitrogen mustard prodrugs for suicide gene therapy)
RN 180839-20-7 HCAPLUS
CN L-Glutamic acid, N-[[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenoxy]carbonyl]-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

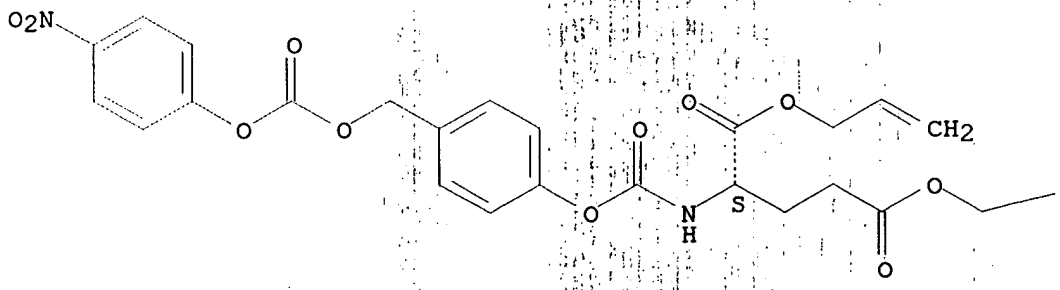
Absolute stereochemistry.



RN 180839-21-8 HCAPLUS
CN L-Glutamic acid, N-[[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenoxy]carbonyl]-, di-2-propenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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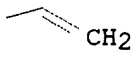

L27 ANSWER 5 OF 24 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:147326 HCAPLUS
DN 128:205147

TI Preparation of non-peptide bombesin receptor antagonists
IN Horwell, David Christopher; Pritchard, Martyn Clive
PA Warner-Lambert Company, USA; Horwell, David Christopher; Pritchard, Martyn Clive
SO PCT Int. Appl., 112 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D401-12
ICS A61K031-395; C07D209-20; C07D213-89; C07D213-40; C07D213-56; C07D405-12; C07D417-12
CC 34-3 (**Amino Acids, Peptides,** and **Proteins**)
Section cross-reference(s): 1
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
BR 9711342	A	19990817	BR 1997-11342	19970222
AU 9741466	A1	19980306	AU 1997-41466	19970806
AU 733226	B2	20010510		
EP 920424	A1	19990609	EP 1997-939359	19970806
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JP 2001500850	T2	20010123	JP 1998-510779	19970806
US 6194437	B1	20010227	US 1999-230933	19990203
NO 9900788	A	19990219	NO 1999-788	19990219
PRAI US 1996-24323	P	19960822		
WO 1997-US13871	W	19970806		

OS MARPAT 128:205147
AB Compds. Ar(CR1R8)0-1(CH2)0-1NR4CONR5CR7(CH2Ar1)CONR6(CH2)0-3(CR2R9)0-1(CH2)0-2R3 [Ar = Ph, (un)substituted pyridyl; R1, R2 = H, alkyl, cycloalkyl; R8, R9 = H or forms a ring with R1 or R2, resp; Ar1 = Ar or pyridyl-N-oxide, indolyl, pyridyl, imidazole; R4, R5, R6, R7 = H, Me; R3 = Ar or H, OH, Me2N, N-methylpyrrole, etc.] or their pharmaceutically acceptable salts were prepd. as bombesin receptor antagonists. Thus, 2-[3-(2,6-diisopropylphenyl)ureido]-3-(1H-indol-3-yl)-2-methyl-N-(1-pyridin-2-ylcyclohexylmethyl)propionamide was prepd. by condensation of .alpha.-methyl-L-tryptophan with 2,6-diisopropylphenyl isocyanate, followed by amidation with 1-pyridin-2-ylcyclohexylmethylamine. Affinity binding data (IC50 values) for the product were detd. to be 5 and <10 nM for the NMB and GRP receptors, resp.
ST pseudopeptide prepn bombesin receptor antagonist
IT Bombesin receptors
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(prepn. of non-peptide bombesin receptor antagonists)
IT Peptides, preparation
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(pseudopeptides; prepn. of non-peptide bombesin receptor antagonists)
IT 204066-87-5P 204067-04-9P
RL: BAC (Biological activity or effector, except adverse); RCT (Reactant);

SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of non-peptide bombesin receptor antagonists)

IT 142627-75-6P 185215-75-2P 204066-70-6P 204066-71-7P 204066-72-8P
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204066-78-4P 204066-79-5P 204066-80-8P 204066-81-9P 204066-82-0P
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204067-01-6P 204067-02-7P 204067-03-8P 204067-05-0P 204067-06-1P
204067-38-9P 204067-40-3P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of non-peptide bombesin receptor antagonists)

IT 204067-30-1P
RL: BYP (Byproduct); PREP (Preparation)
(prepn. of non-peptide bombesin receptor antagonists)

IT 54-12-6, Tryptophan 62-53-3, Benzenamine, reactions 73-22-3, L-Tryptophan, reactions 100-28-7, p-Nitrophenyl isocyanate 111-24-0, 1,5-Dibromopentane 153-91-3, Tryptophan, .alpha.-methyl- 487-59-2 1121-78-4 1206-13-9 1548-13-6 2739-97-1, 2-Pyridylacetonitrile 3218-02-8, Cyclohexanemethanamine 4000-72-0 4442-85-7, 2-Cyclohexylethylamine 5766-79-0 7693-46-1, p-Nitrophenyl chloroformate 16709-25-4, .alpha.-Methyl-L-tryptophan 17540-18-0 18502-05-1, 4-Imidazoleacetonitrile 23357-52-0 24544-04-5, 2,6-Diisopropylaniline 25756-29-0, n-Methylcyclohexylmethylamine 28178-42-9, 2,6-Diisopropylphenyl isocyanate 30806-83-8 35019-66-0 40465-45-0 50528-53-5 56452-52-9 61341-86-4, s 1-Aminoindan 70258-01-4 81428-13-9 103110-98-1 114524-80-0 114779-79-2 135207-25-9 142854-50-0 164323-86-8 204067-18-5 204067-20-9 204067-24-3 204067-28-7
RL: RCT (Reactant)
(prepn. of non-peptide bombesin receptor antagonists)

IT 5815-73-6P 13139-14-5P 13458-33-8P 35392-66-6P 37982-29-9P
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135627-41-7P 135627-42-8P 142946-11-0P 187610-49-7P 187610-50-0P
190333-61-0P 204067-07-2P 204067-08-3P 204067-09-4P 204067-10-7P
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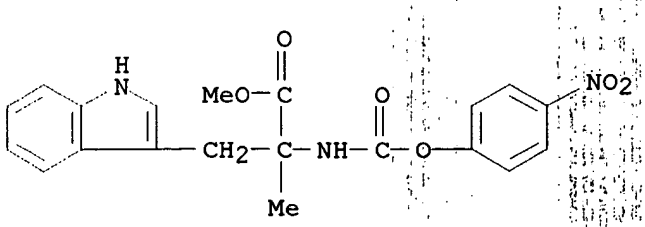
204067-16-3P 204067-17-4P 204067-19-6P 204067-21-0P 204067-22-1P
204067-23-2P 204067-25-4P 204067-26-5P **204067-27-6P**
204067-29-8P 204067-31-2P 204067-32-3P 204067-33-4P 204067-34-5P
204067-35-6P 204067-36-7P 204067-37-8P 204067-39-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of non-peptide bombesin receptor antagonists)

IT **204067-27-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of non-peptide bombesin receptor antagonists)

RN 204067-27-6 HCAPLUS
CN Tryptophan, .alpha.-methyl-N-[(4-nitrophenoxy)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)



L27 ANSWER 6 OF 24 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:17976 HCAPLUS
DN 128:61798
TI Preparation of epoxide peptidomimetics as irreversible HIV protease inhibitors
IN Yoon, Heungsik; Choy, Nakyen; Kim, Sung Chun; Choi, Ho Il; Son, Young Chan; Park, Chi Hyo; Moon, Kwang-yul; Jung, Wonhee; Kim, Chung Ryeol; Lee, Chang Sun; Koh, Jong Sung; Kim, Sang Soo
PA LG Chemical Ltd., S. Korea
SO U.S., 50 pp. Cont.-in-part of U.S. Ser. No. 341,352, abandoned.
CODEN: USXXAM
DT Patent
LA English
IC ICM A61K031-44
ICS A61K031-47
NCL 514314000
CC 34-3 (**Amino Acids, Peptides,** and **Proteins**)
Section cross-reference(s): 1, 63
FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5696134	A	19971209	US 1995-473877	19950607
	US 5587388	A	19961224	US 1993-159382	19931130
	KR 125117	B1	19971205	KR 1994-13423	19940615
	US 5773468	A	19980630	US 1995-572402	19951214
	US 5744621	A	19980428	US 1996-667888	19960620
	US 5763631	A	19980609	US 1996-667133	19960620
PRAI	US 1993-159382	A2	19931130		
	KR 1994-13423	A	19940615		
	US 1994-341352	B2	19941117		
	KR 1992-23088	A	19921202		
	KR 1992-23089	A	19921202		
	KR 1993-10811	A	19930614		
	KR 1993-21298	A	19931014		
	KR 1993-21299	A	19931014		
	KR 1993-21300	A	19931014		
	US 1995-473877	A2	19950607		
	KR 1995-37292	A	19951026		

OS MARPAT 128:61798
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Novel cis-epoxide compds. I [R1, R2 = independently H, alkyl; R3 = aryl or alkyl (un)substituted with arom., C3-8 cycloalkyl; R4 = H, C1-4 alkyl; n = 0-2; X = CO, COCO, S(O), SO2, CS; Y = O, CH2, NH, NMe; m = 0, 1; R5 = heterocycle; straight, branched, or cyclic C1-8 alkyl; alkyl substituted with heterocycle or cycloalkyl; straight, branched, or cyclic C1-8 alkoxy; aryl-substituted alkoxy; NR6R7; R6 = straight or branched C1-8 alkyl, cycloalkyl, alkyl substituted with cycloalkyl; R7 = H, alkyl; Z = O, NH, NMe; R8, R9 = independently alkyl (un)substituted with arom. hydrocarbon or cycloalkyl; C3-8 cycloalkyl; arom.] are useful for treating or preventing diseases caused by HIV infection. The novel HIV protease inhibitors I have specific structures to form stable bonding with the enzyme active site, which entails a highly enhanced irreversible

inhibition against HIV protease. Thus deprotection and peptide coupling of olefin II (prepd. in 4 steps from protected L-phenylalaninal and (S)-2-amino-3-methyl-1-phenylbutane) with penicillamine-derived sulfone III (prepd. in 3 steps from L-penicillamine), followed by epoxidn. with mCPBA gave title epoxide deriv. IV. IV showed irreversible inactivation of HIV-1 protease, with a stoichiometric ratio of inhibitor to enzyme of 1:1. IV also showed antiviral activity against HIV-1 with IC50 = 1 nM.

ST epoxide peptidomimetic prepn HIV protease inhibitor; virucide HIV epoxide peptidomimetic prepn; AIDS treatment epoxide peptidomimetic prepn; immunomodulator epoxide peptidomimetic prepn

IT Peptidomimetics
(epoxide; prepn. of epoxide peptidomimetics as irreversible HIV protease inhibitors)

IT Epoxides
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(peptidomimetics; prepn. of epoxide peptidomimetics as irreversible HIV protease inhibitors)

IT Anti-AIDS drugs
Antiviral agents
Human immunodeficiency virus 1
Immunomodulators
(prepn. of epoxide peptidomimetics as irreversible HIV protease inhibitors)

IT 174562-29-9P 174562-30-2P 174562-31-3P 174562-32-4P 174562-33-5P
174562-34-6P 174562-35-7P 174562-36-8P 174562-37-9P 174562-38-0P
174562-39-1P 174562-40-4P 174562-41-5P 174562-42-6P 174562-43-7P
174562-44-8P 174562-45-9P 174562-46-0P 174562-47-1P 174562-48-2P
174562-49-3P 174562-50-6P 174562-51-7P 174562-52-8P 174562-53-9P
174562-54-0P 174562-55-1P 174562-56-2P 174562-57-3P 174562-58-4P
174562-59-5P 174562-60-8P 174562-61-9P 174562-62-0P 174562-63-1P
174562-65-3P 174562-66-4P 174562-67-5P 174562-68-6P 174562-69-7P
174562-70-0P 174562-71-1P 174562-72-2P 174562-73-3P 174562-74-4P
174562-75-5P 174562-76-6P 174562-77-7P 174562-78-8P 174562-79-9P
174562-80-2P 174562-81-3P 200262-27-7P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of epoxide peptidomimetics as irreversible HIV protease inhibitors)

IT 144114-21-6, Retropepsin
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(prepn. of epoxide peptidomimetics as irreversible HIV protease inhibitors)

IT 59-67-6, 3-Pyridinecarboxylic acid, reactions 78-77-3, Isobutyl bromide 78-82-0, Isobutyronitrile 88-14-2, 2-Furancarboxylic acid 93-10-7, 2-Quinolinecarboxylic acid 96-41-3, Cyclopentanol 98-00-0, 2-Furanylmethanol 98-59-9, p-Toluenesulfonyl chloride 98-98-6, 2-Pyridinecarboxylic acid 100-46-9, Benzylamine, reactions 100-55-0, 3-Pyridylcarbinol 110-68-9, N-Methyl-N-butylamine 503-74-2, Isovaleric acid 527-72-0, 2-Thiophenecarboxylic acid 574-98-1, N-(2-Bromoethyl)phthalimide 586-95-8, 4-Pyridylcarbinol 586-98-1, 2-Pyridylcarbinol 603-35-0, Triphenylphosphine, reactions 617-89-0, 2-Furanylmethylamine 625-45-6, Methoxyacetic acid 1113-41-3, L-Penicillamine 2516-33-8, Cyclopropylmethanol 4083-57-2, 3-Amino-2,4-dimethylpentane 5163-20-2, N-Methyl-N-cyclopropylamine 6921-34-2, Benzylmagnesium chloride 6964-21-2, 3-Thiopheneacetic acid 7693-46-1, p-Nitrophenyl chloroformate 13734-34-4 23844-66-8 24939-24-0, p-Aminobenzenesulfonyl chloride 33445-07-7, Isopropoxyacetic

acid 59830-60-3, N-Benzyloxycarbonyl-L-phenylalaninal 80866-93-9
96521-86-7 96928-87-9 111491-96-4 123617-80-1, 3-Furanacetic acid
136465-98-0
RL: RCT (Reactant)
(prepn. of epoxide peptidomimetics as irreversible HIV protease inhibitors)

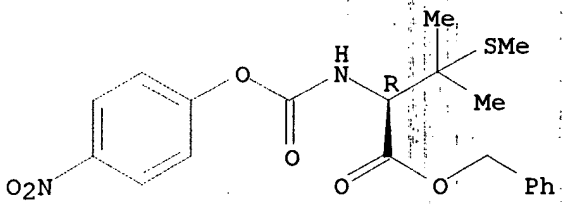
IT 65273-64-5P 82894-53-9P 97589-56-5P 112898-22-3P 156641-79-1P
156641-81-5P 156641-83-7P 160742-44-9P 160742-45-0P 160742-70-1P
160742-71-2P 174562-82-4P 174562-83-5P 174562-84-6P 174562-85-7P
174562-86-8P 174562-88-0P 174562-89-1P 174562-90-4P
174562-91-5P 174562-92-6P 174562-94-8P 196515-98-7P
200262-28-8P 200262-29-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of epoxide peptidomimetics as irreversible HIV protease inhibitors)

IT 156715-06-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of epoxide peptidomimetics as irreversible HIV protease inhibitors)

IT **174562-91-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of epoxide peptidomimetics as irreversible HIV protease inhibitors)

RN 174562-91-5 HCAPLUS
CN L-Valine, 3-(methylthio)-N-[(4-nitrophenoxy)carbonyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L27 ANSWER 7 OF 24 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:440050 HCAPLUS
DN 127:66223
TI Preparation of urea moiety-containing peptide derivatives as neutral endopeptidase and angiotensin converting enzyme inhibitors
IN Nagano, Masanobu; Takenaka, Yasuhei; Kato, Takeshi
PA Fujisawa Pharmaceutical Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 51 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
IC ICM C07C275-16
ICS A61K031-195; A61K031-215; A61K031-445; A61K038-00; C07C275-18; C07D207-06; C07D207-16; C07D211-62; A61K031-40; C12N009-99; C07M007-00
CC 34-3 (**Amino Acids, Peptides,** and **Proteins**)
Section cross-reference(s): 1

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI JP 09118662 A2 19970506 JP 1996-237543 19960909
PRAI GB 1995-18553 19950911
OS MARPAT 127:66223
AB The title compds. R1CONHACHR2YNR3CONR4CHR6R5 [R1 = heterocyclic ring, etc.; R2 = carboxy, etc.; R3 = alkyl, etc.; R5 = carboxy, etc.; A = alkylene; Y = alkylene; R4 = H, etc.; R6 = (aryl-substituted) alkyl, etc.] are prepd. (2R or 2S)-N-[N-butyl-N-[2-carboxy-3-[(S)-prolylamino]propyl]carbamoyl]-4-phenyl-(S)-phenylalanine trifluoroacetic acid salt (prepn. given) in vitro showed IC50 of 7.2 x 10-8 M against neutral endopeptidase.
ST ureidopeptide prepn neutral endopeptidase inhibitor; angiotensin converting enzyme inhibitor ureidopeptide prepn; antihypertensive ureidopeptide prepn prepn
IT Anti-inflammatory drugs
Antihypertensives
RL: SPN (Synthetic preparation); PREP (Preparation)
(urea moiety-contg. peptide derivs. with neutral endopeptidase and angiotensin converting enzyme inhibiting activity)
IT 191422-90-9P 191422-91-0P 191422-92-1P 191422-93-2P 191422-94-3P
191422-96-5P 191422-98-7P 191422-99-8P 191423-01-5P 191423-02-6P
191423-03-7P 191423-04-8P 191423-05-9P 191423-06-0P 191423-07-1P
191423-08-2P 191423-09-3P 191423-10-6P 191423-11-7P 191423-12-8P
191423-13-9P 191423-14-0P 191423-15-1P 191423-16-2P 191423-17-3P
191423-18-4P 191423-19-5P 191423-20-8P 191423-21-9P 191423-22-0P
191423-24-2P 191423-26-4P 191423-28-6P 191423-30-0P 191423-32-2P
191423-34-4P 191423-36-6P 191423-38-8P 191423-40-2P 191423-42-4P
191423-44-6P 191423-46-8P 191423-48-0P 191423-50-4P 191423-52-6P
191423-54-8P 191423-56-0P 191423-58-2P 191423-60-6P 191423-62-8P
191423-64-0P 191423-66-2P 191423-68-4P 191423-70-8P 191423-72-0P
191423-74-2P 191423-76-4P 191423-78-6P 191423-79-7P 191423-80-0P
191423-81-1P 191423-83-3P 191423-85-5P 191423-87-7P 191423-89-9P
191423-91-3P 191423-93-5P 191423-95-7P 191423-96-8P 191423-97-9P
191423-98-0P 191423-99-1P 191424-00-7P 191424-01-8P 191424-02-9P
191424-03-0P 191424-04-1P 191424-05-2P 191424-06-3P 191424-07-4P
191424-08-5P 191424-09-6P 191424-10-9P 191424-12-1P 191424-13-2P
191424-14-3P 191424-15-4P 191424-17-6P 191424-18-7P 191424-19-8P
191424-21-2P 191424-23-4P 191424-24-5P 191424-27-8P 191424-28-9P
191424-29-0P 191424-31-4P 191424-32-5P 191424-33-6P 191424-34-7P
191424-37-0P 191424-40-5P 191424-42-7P 191424-45-0P 191424-48-3P
191424-50-7P 191424-53-0P 191424-56-3P 191424-59-6P 191424-61-0P
191424-63-2P 191424-65-4P 191424-67-6P 191424-69-8P 191424-70-1P
191424-73-4P 191424-75-6P 191424-77-8P 191424-80-3P 191424-82-5P
191424-84-7P 191424-86-9P 191424-88-1P 191424-90-5P 191424-92-7P
191424-93-8P 191424-94-9P 191424-96-1P 191424-98-3P 191425-00-0P
191425-02-2P 191425-04-4P 191425-06-6P 191425-08-8P 191425-10-2P
191425-12-4P 191425-13-5P 191425-14-6P 191425-16-8P 191425-18-0P
191425-19-1P 191425-21-5P 191425-23-7P 191425-24-8P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of urea moiety-contg. peptide derivs. as neutral endopeptidase and angiotensin converting enzyme inhibitors)
IT 9015-82-1, Angiotensin converting enzyme 82707-54-8, Neutral endopeptidase
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(prepn. of urea moiety-contg. peptide derivs. as neutral endopeptidase and angiotensin converting enzyme inhibitors)
IT 75-36-5, Acetyl chloride 95-56-7, 2-Bromophenol 100-39-0, Benzyl bromide 109-73-9, Butylamine, reactions 123-72-8, Butylaldehyde

123-75-1, Pyrrolidine, reactions 617-52-7, Dimethyl itaconate 2812-46-6 5419-55-6, Triisopropyl borate 6165-69-1, 3-Thienylboronic acid 7693-46-1 9000-92-4, Amylase 24424-99-5, Di-tert-butyl dicarbonate 28310-65-8 30418-59-8, 3-Aminophenylboronic acid 32315-10-9, Triphosgene 63024-30-6 71989-31-6 118786-32-6
191426-93-4 191426-94-5
RL: RCT (Reactant)
(prepn. of urea moiety-contg. peptide derivs. as neutral endopeptidase and angiotensin converting enzyme inhibitors)

IT 6793-92-6P 31575-75-4P 53087-13-1P 78887-39-5P 118602-51-0P
118602-52-1P 137255-87-9P 137255-91-5P 146631-00-7P 150351-64-7P
156682-54-1P 190661-29-1P 191425-25-9P **191425-26-0P**
191425-27-1P 191425-28-2P 191425-29-3P 191425-30-6P 191425-31-7P
191425-32-8P 191425-33-9P 191425-34-0P 191425-35-1P 191425-36-2P
191425-37-3P 191425-38-4P 191425-39-5P 191425-40-8P
191425-41-9P 191425-42-0P 191425-43-1P 191425-44-2P 191425-45-3P
191425-46-4P 191425-47-5P 191425-48-6P 191425-49-7P 191425-50-0P
191425-51-1P 191425-52-2P 191425-53-3P 191425-54-4P
191425-55-5P 191425-56-6P 191425-57-7P
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191425-61-3P 191425-62-4P 191425-63-5P 191425-64-6P 191425-65-7P
191425-66-8P 191425-67-9P 191425-68-0P 191425-69-1P 191425-70-4P
191425-71-5P 191425-72-6P 191425-73-7P 191425-74-8P 191425-75-9P
191425-77-1P 191425-79-3P 191425-81-7P 191425-83-9P 191425-85-1P
191425-87-3P 191425-88-4P 191425-90-8P 191425-92-0P 191425-94-2P
191425-95-3P 191425-97-5P 191426-01-4P 191426-03-6P 191426-05-8P
191426-07-0P 191426-09-2P 191426-11-6P 191426-13-8P 191426-15-0P
191426-16-1P 191426-17-2P 191426-18-3P 191426-21-8P 191426-23-0P
191426-26-3P 191426-27-4P 191426-29-6P
191426-31-0P 191426-33-2P 191426-35-4P 191426-37-6P
191426-39-8P 191426-40-1P 191426-41-2P 191426-42-3P 191426-43-4P
191426-44-5P 191426-45-6P 191426-46-7P 191426-47-8P 191426-48-9P
191426-49-0P 191426-50-3P 191426-51-4P 191426-52-5P 191426-53-6P
191426-54-7P 191426-55-8P 191426-56-9P 191426-57-0P 191426-58-1P
191426-59-2P 191426-60-5P 191426-61-6P 191426-62-7P 191426-63-8P
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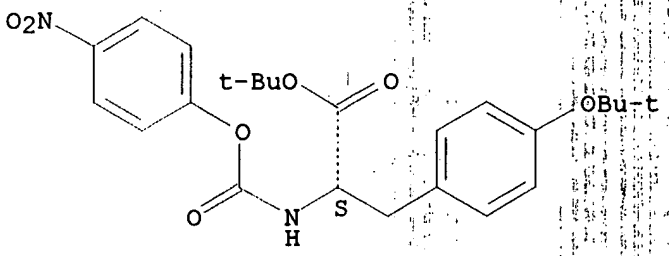
191426-71-8P 191426-72-9P 191426-73-0P 191426-74-1P
191426-75-2P 191426-76-3P 191426-77-4P
191426-78-5P 191426-80-9P 191426-81-0P 191426-82-1P
191426-83-2P 191426-84-3P 191426-85-4P 191426-86-5P
191426-87-6P 191426-88-7P 191426-89-8P 191426-90-1P
191426-91-2P 191426-92-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of urea moiety-contg. peptide derivs. as neutral endopeptidase and angiotensin converting enzyme inhibitors)

IT **191426-93-4**
RL: RCT (Reactant)
(prepn. of urea moiety-contg. peptide derivs. as neutral endopeptidase and angiotensin converting enzyme inhibitors)

RN 191426-93-4 HCAPLUS
CN L-Tyrosine, O-(1,1-dimethylethyl)-N-[(4-nitrophenoxy)carbonyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

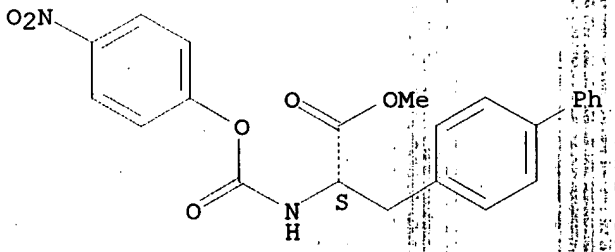
Absolute stereochemistry.



IT **191425-26-0P 191425-37-3P 191425-55-5P**
191425-56-6P 191425-57-7P 191425-58-8P
191425-59-9P 191425-60-2P 191426-26-3P
191426-27-4P 191426-29-6P 191426-31-0P
191426-75-2P 191426-76-3P 191426-77-4P
191426-78-5P 191426-87-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of urea moiety-contg. peptide derivs. as neutral endopeptidase and angiotensin converting enzyme inhibitors)

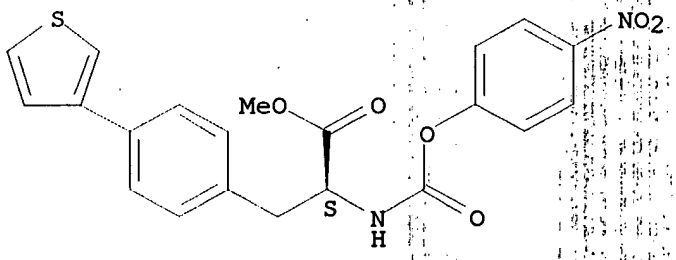
RN 191425-26-0 HCAPLUS
CN [1,1'-Biphenyl]-4-propanoic acid, .alpha.-[[(4-nitrophenoxy)carbonyl]amino]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



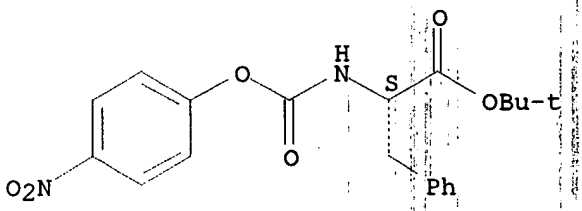
RN 191425-37-3 HCAPLUS
CN L-Phenylalanine, N-[(4-nitrophenoxy)carbonyl]-4-(3-thienyl)-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



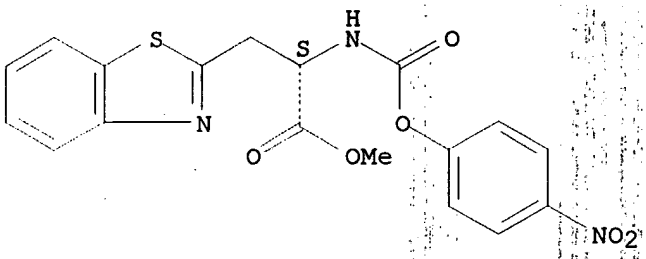
RN 191425-55-5 HCAPLUS
CN L-Phenylalanine, N-[(4-nitrophenoxy)carbonyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



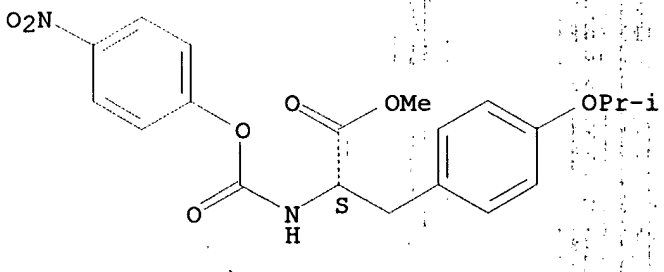
RN 191425-56-6 HCAPLUS
CN 2-Benzothiazolepropanoic acid, .alpha.-[[(4-nitrophenoxy)carbonyl]amino]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



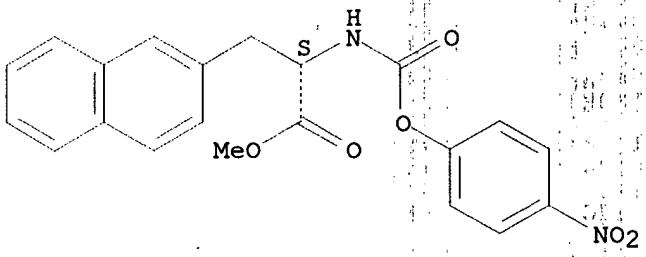
RN 191425-57-7 HCAPLUS
CN L-Tyrosine, O-(1-methylethyl)-N-[(4-nitrophenoxy)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



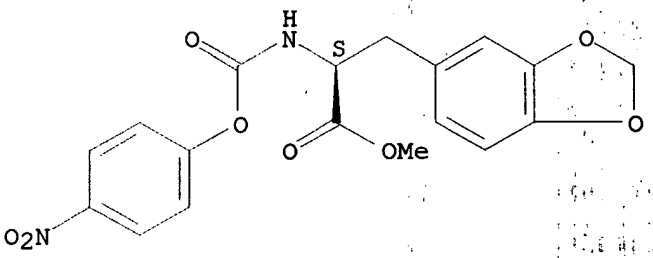
RN 191425-58-8 HCAPLUS
CN 2-Naphthalenepropanoic acid, .alpha.-[[(4-nitrophenoxy)carbonyl]amino]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



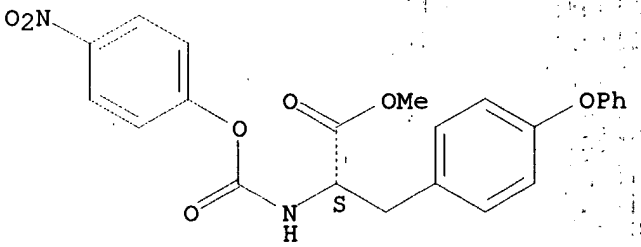
RN 191425-59-9 HCAPLUS
CN 1,3-Benzodioxole-5-propanoic acid, .alpha.-[[(4-nitrophenoxy)carbonyl]amino]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



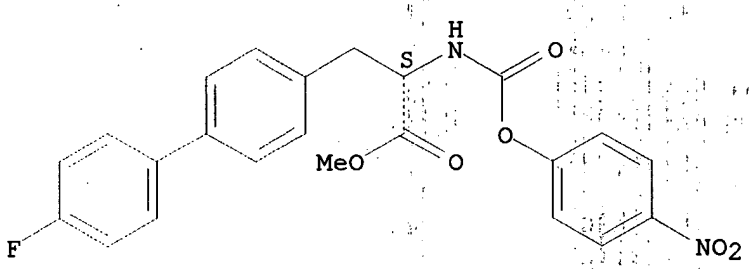
RN 191425-60-2 HCAPLUS
CN L-Tyrosine, N-[(4-nitrophenoxy)carbonyl]-O-phenyl-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



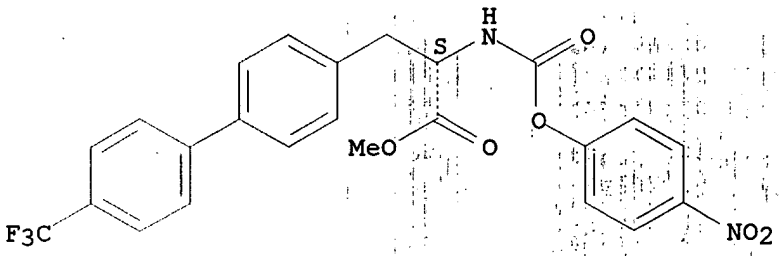
RN 191426-26-3 HCAPLUS
CN [1,1'-Biphenyl]-4-propanoic acid, 4'-fluoro-.alpha.-[[(4-nitrophenoxy)carbonyl]amino]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



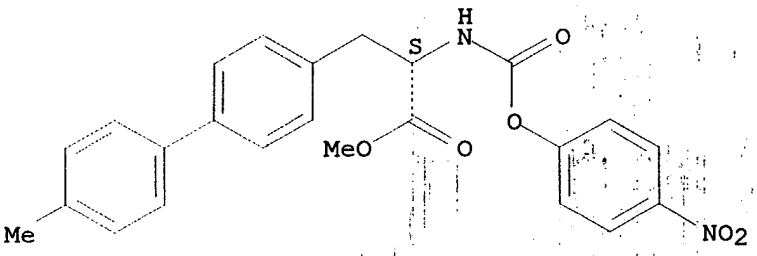
RN 191426-27-4 HCAPLUS
CN [1,1'-Biphenyl]-4-propanoic acid, .alpha.-[[(4-nitrophenoxy)carbonyl]amino]-4'-(trifluoromethyl)-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



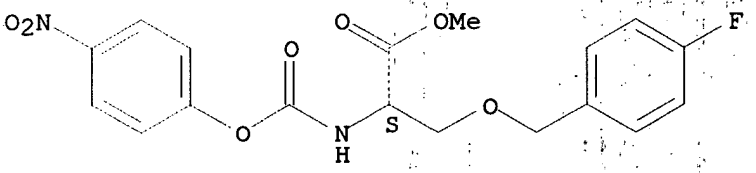
RN 191426-29-6 HCAPLUS
CN [1,1'-Biphenyl]-4-propanoic acid, 4'-methyl-.alpha.-[[(4-nitrophenoxy)carbonyl]amino]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



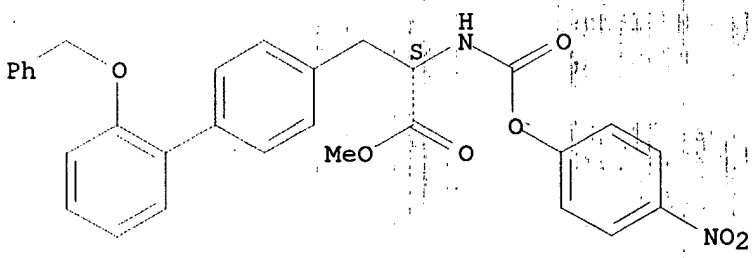
RN 191426-31-0 HCAPLUS
CN L-Serine, O-[(4-fluorophenyl)methyl]-N-[(4-nitrophenoxy)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



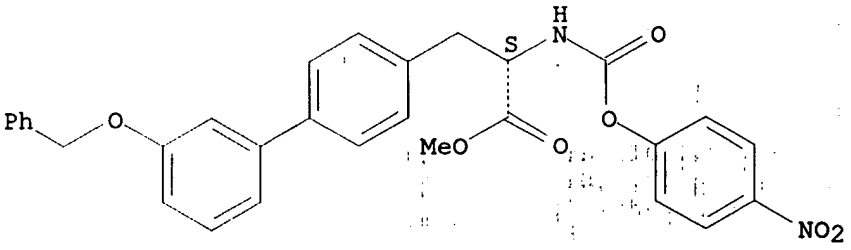
RN 191426-75-2 HCAPLUS
CN [1,1'-Biphenyl]-4-propanoic acid, .alpha.-[[(4-nitrophenoxy)carbonyl]amino]-2'-(phenylmethoxy)-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



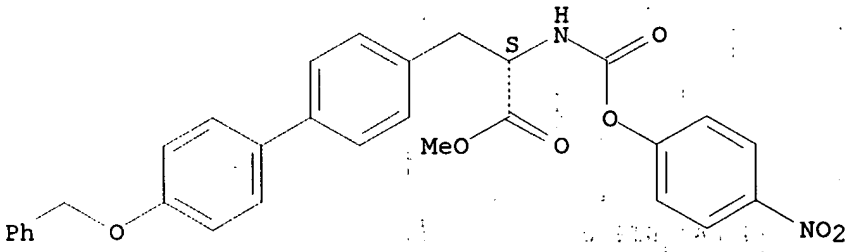
RN 191426-76-3 HCAPLUS
CN [1,1'-Biphenyl]-4-propanoic acid, .alpha.-[[(4-nitrophenoxy)carbonyl]amino]-3'-(phenylmethoxy)-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



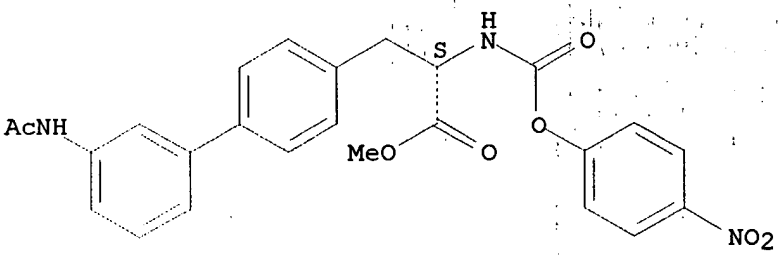
RN 191426-77-4 HCAPLUS
CN [1,1'-Biphenyl]-4-propanoic acid, .alpha.-[[(4-nitrophenoxy)carbonyl]amino]-4'-(phenylmethoxy)-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



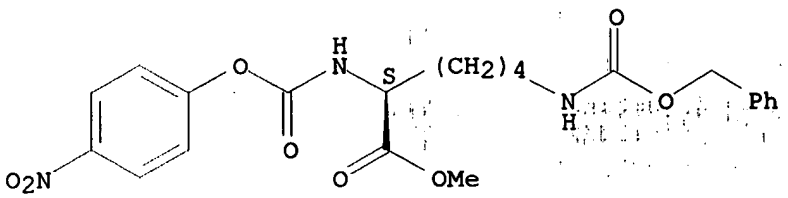
RN 191426-78-5 HCAPLUS
CN [1,1'-Biphenyl]-4-propanoic acid, 3'-(acetylamino)-.alpha.-[[(4-nitrophenoxy)carbonyl]amino]-, methyl ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 191426-87-6 HCAPLUS
CN L-Lysine, N2-[(4-nitrophenoxy)carbonyl]-N6-[(phenylmethoxy)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L27 ANSWER 8 OF 24 HCAPLUS COPYRIGHT 2001 ACS
AN 1996:637443 HCAPLUS
DN 125:329473
TI Preparation of aminediol-containing peptide analogs as retroviral protease inhibitors
IN Gordon, Eric M.; Barrish, Joel C.; Bisacchi, Gregory S.; Sun, Chong-qing; Tino, Joseph A.; Vite, Gregory D.; Zahler, Robert
PA E. R. Squibb & Sons, Inc., USA
SO U.S., 219 pp. Cont.-in-part of U.S. Ser. No. 927,027, abandoned.
CODEN: USXXAM
DT Patent
LA English
IC ICM C07D401-12
NCL 552303000
CC 34-3 (**Amino Acids, Peptides,** and **Proteins**)
Section cross-reference(s): 1
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5559256	A	19960924	US 1993-79978	19930625
	AU 9341659	A1	19940127	AU 1993-41659	19930630
	AU 677194	B2	19970417		
	HU 67090	A2	19950130	HU 1993-2080	19930719
	CA 2100894	AA	19940121	CA 1993-2100894	19930720
	NO 9302620	A	19940121	NO 1993-2620	19930720
	EP 580402	A2	19940126	EP 1993-305691	19930720
	EP 580402	A3	19970305		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	ZA 9305243	A	19940217	ZA 1993-5243	19930720
	CN 1085546	A	19940420	CN 1993-108954	19930720
	JP 06206857	A2	19940726	JP 1993-201016	19930720
	US 5760036	A	19980602	US 1995-455295	19950531
	US 5776933	A	19980707	US 1995-456125	19950531
PRAI	US 1992-916916		19920720		
	US 1992-927027		19920806		
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OS MARPAT 125:329473
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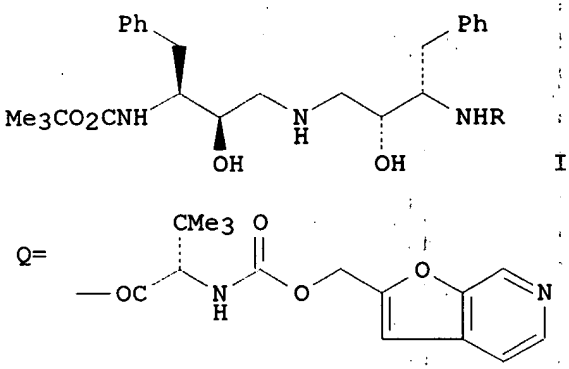

AB Aa-E-NR8CHR9H(OH)CH2NHCH2CH(OH)CHR9NR8-E-Ab [Aa, Ab = H, alkyl, R3C(:Z), R3SO2, R3R4NSO2, R3R4NC(:Z), R3SC(:O), R5R6R7COC(:Z); E = a single bond or a peptide chain contg. 1 to 4 amino acids, the N-terminus of which is bonded to Aa or Ab; R3, R4 = H, alkyl, aryl, carbocyclyl; R5, R6, R7 = H, alkyl, aryl, carbocyclyl, fluorenyl, alkynyl, alkenyl; R5, R6, and R7 may, independently, be joined together with the carbon atom to which they are bonded, to form a mono-, bi- or tricyclic carbocyclic ring system; R8 = H, alkyl; R9 = arylalkyl; Z = O, S; wherein: wherever they appear alone or as part of another group, unless otherwise indicated, the terms "alk." or "alkyl" denote a straight or branched chain satd. radical contg. 1 to 12 carbons in the normal chain, optionally substituted by one or more groups selected from (un)protected OH, oxo (with the proviso that the carbon bearing the oxo group is not adjacent to a heteroatom), CO2H, halo, alkoxy, aryloxy, alkoxycarbonyl, etc.] or salts thereof, which inhibit retroviral protease and are particularly useful in the treatment and/or prevention of HIV infection (AIDS), are prepd. Thus, bis(3-amino-2-hydroxy-4-phenylbutyl)amine deriv. (I; R = H) was condensed with L-tert-leucine deriv. (HO-Q) using 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride and HOBT in DMF/CH2CH2 at 0.degree. to room temp. to give the title compd. I (R = Q). The latter compd. at 10 .mu.M in vitro inhibited 99% HIV protease and showed IC50 of 0.012 .mu.M which was the concn. of drug that increased the formazan prodn. in CEM-SS cells infected with the RF strain of HIV to 50% of that produced by uninfected cells in the absence of drug.

ST aminediol contg peptide analog prepn; retroviral protease inhibitor; HIV infection AIDS treatment

IT Acquired immune deficiency syndrome
Virucides and Virustats
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of aminediol-contg. peptide analogs as retroviral protease inhibitors for treatment of HIV infection (AIDS))

IT Peptides, preparation
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(analogs, prepn. of aminediol-contg. peptide analogs as retroviral protease inhibitors for treatment of HIV infection (AIDS))

IT Virus, animal
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(human immunodeficiency, prepn. of aminediol-contg. peptide analogs as retroviral protease inhibitors for treatment of HIV infection (AIDS))

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RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of aminediol-contg. peptide analogs as retroviral protease inhibitors for treatment of HIV infection (AIDS))

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RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of aminediol-contg. peptide analogs as retroviral protease inhibitors for treatment of HIV infection (AIDS))

IT 144114-21-6, Retropepsin
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)
(prepn. of aminediol-contg. peptide analogs as retroviral protease inhibitors for treatment of HIV infection (AIDS))

IT 50-00-0, Formaldehyde, reactions 52-52-8, 1-Aminocyclopentanecarboxylic acid 56-12-2, 4-Aminobutyric acid, reactions 64-18-6, Formic acid, reactions 68-12-2, Dimethylformamide, reactions 70-25-7 72-18-4, L-Valine, reactions 74-88-4, Methyl iodide, reactions 74-89-5, Methylamine, reactions 75-16-1, Methylmagnesium bromide 75-36-5, Acetyl chloride 75-44-5, Phosgene 75-66-1, tert-Butyl mercaptan 75-98-9, Trimethylacetic acid 76-83-5, Triphenylmethyl chloride 77-76-9, 2,2-Dimethoxypropane 79-14-1, reactions 79-22-1, Methyl chloroformate 79-44-7, Dimethylcarbamyl chloride 79-50-5, DL-Pantolactone 83-33-0, 1-Indanone 91-62-3, 6-Methylquinoline 93-10-7, Quinaldic acid 95-54-5, o-Phenylenediamine, reactions 95-55-6, o-Aminophenol 96-49-1, Ethylene carbonate 98-59-9, Tosyl chloride 98-80-6, Phenylboronic acid 98-88-4, Benzoyl chloride 100-39-0, Benzyl bromide 100-44-7, Benzyl chloride, reactions 100-46-9, Benzylamine, reactions 100-52-7, Benzaldehyde, reactions 100-86-7, .alpha.,.alpha.-Dimethylphenethyl alcohol 103-74-2, 2-(2-Hydroxyethyl)pyridine 105-36-2, Ethyl bromoacetate 108-23-6, Isopropyl chloroformate 108-24-7, Acetic anhydride 109-00-2, 3-Hydroxypyridine 109-86-4, 2-Methoxyethanol 110-06-5, tert-Butyl

disulfide 110-15-6, Butanedioic acid, reactions 110-91-8, Morpholine, reactions 111-42-2, reactions 119-67-5, 2-Carboxybenzaldehyde 122-59-8, Phenoxyacetic acid 122-98-5, 2-Anilinoethanol 122-99-6, 2-Phenoxyethanol 137-07-5, 2-Aminothiophenol 288-32-4, Imidazole, reactions 335-08-0, 1,1,1-Trifluoroacetone cyanohydrin 353-80-0 358-23-6, Triflic anhydride 453-20-3, 3-Hydroxytetrahydrofuran 473-85-8, 1,4-Anhydro-D-threitol 500-22-1, 3-Pyridinecarboxaldehyde 501-53-1, Benzyl chloroformate 503-38-8, Trichloromethyl chloroformate 534-03-2, 2-Amino-1,3-propanediol 539-74-2, Ethyl 3-bromopropionate 540-51-2, 2-Bromoethanol 541-47-9, 3,3-Dimethylacrylic acid 558-30-5, Isobutylene oxide 586-98-1, 2-Pyridylcarbinol 591-80-0, 4-Pentenoic acid 593-56-6, Methoxyamine hydrochloride 594-56-9, 2,3,3-Trimethylbutene 598-21-0, Bromoacetyl bromide 611-71-2 617-35-6, Ethyl pyruvate 617-94-7, Dimethylphenyl carbinol 622-08-2, 2-Benzyloxyethanol 622-40-2, 4-(2-Hydroxyethyl)morpholine 623-08-5, N-Methyl-p-toluidine 624-83-9, Methyl isocyanate 625-38-7, 3-Butenoic acid 627-18-9 628-41-1, 1,4-Cyclohexadiene 630-19-3, Pivalaldehyde 644-36-0, o-Tolylacetic acid 670-95-1, 4-Phenylimidazole 672-15-1, L-Homo-serine 677-22-5, tert-Butylmagnesium chloride 687-47-8, (S)-Ethyl lactate 693-89-0, 1-Methylcyclopentene 759-24-0, Diethyl tert-butylmalonate 775-06-4, DL-Meta-tyrosine 821-09-0, 4-Penten-1-ol 917-54-4, Methyllithium 937-14-4, m-Chloroperbenzoic acid 1003-04-9 1070-83-3, tert-Butylacetic acid 1120-87-2, 4-Bromopyridine 1122-62-9, 2-Acetylpyridine 1142-20-7 1145-80-8 1148-11-4 1149-26-4 1161-13-3 1193-47-1, 2,2-Dimethylcyclohexanone 1462-03-9, 1-Methyl-1-cyclopentanol 1609-86-5, tert-Butyl isocyanate 1664-54-6, 3-Amino-3-phenylpropionic acid 1779-49-3, Methyltriphenylphosphonium bromide 1826-67-1, Vinylmagnesium bromide 2018-66-8 2130-96-3 2212-75-1 2370-61-8 2976-75-2, (1-Naphthoxy)acetic acid 2987-16-8, 3,3-Dimethylbutyraldehyde 3160-59-6 3173-56-6, Benzyl isocyanate 3240-94-6, 4-(2-Chloroethyl)morpholine 3262-72-4 3587-60-8, Benzyl chloromethyl ether 3731-51-9, 2-(Aminomethyl)pyridine 4436-24-2, Benzyloxirane 4530-20-5 4541-32-6, 2,2-Dimethylcyclopentanone 4857-04-9, 2-(Chloromethyl)benzimidazole 5034-06-0, Trimethylsulfoxonium chloride 5333-74-4, Ethyl tert-butylglyoxylate 5470-11-1, Hydroxylamine hydrochloride 6278-91-7, 4-Benzyloxy-2-butanone 6290-49-9, Methyl methoxyacetate 6306-52-1, L-Valine methyl ester hydrochloride 6351-10-6, 1-Indanol 6829-40-9, Diethyl aminomalonate 7326-19-4, D-Phenyllactic acid 7364-25-2, Indazolinone 7432-21-5 7486-35-3, Vinyltributyltin 7536-55-2 7677-24-9, Trimethylsilyl cyanide 7693-46-1, p-Nitrophenyl chloroformate 10147-11-2, 3-Phenyl-1-propyne 13031-04-4 13139-15-6 13139-16-7 13139-17-8, N-Benzyloxycarbonyloxy succinimide 13329-18-5, 5-Benzyloxy-2-pentanone 13570-08-6, 2-Benzimidazoleacetic acid 13575-16-1, Ethyl 5-Phenyloxazole-2-carboxylate 13734-34-4 13734-41-3 14347-78-5, (R)-2,2-Dimethyl-1,3-dioxolane-4-methanol 14397-64-9, 1-Ethoxycarbonyl-2-indanone 15761-39-4 16520-62-0, 4-Phenyl-1-butyne 16677-29-5 17199-29-0 17392-83-5, (R)-Methyl lactate 17463-43-3, DL-3,3,3-Trifluoroalanine 18162-48-6, tert-Butyldimethylsilyl chloride 18942-49-9 19575-07-6, Methyl quinaldate 19728-63-3, Z-Thr-OH 19752-84-2, 3-Hydroxytetrahydropyran 19810-31-2, Benzyloxyacetyl chloride 20117-47-9, 1-Methyl-1-cyclobutanol 20160-60-5, 2-Trimethylsilylethyl chloroformate 20412-38-8, Neopentyl chloroformate 20662-89-9, 4-Phenyloxazole 20859-02-3, L-tert-Leucine 21641-92-9 22146-57-2 22323-82-6, (S)-2,2-Dimethyl-1,3-dioxolane-4-methanol 24424-99-5, Di-tert-butyl dicarbonate 26628-22-8, Sodium azide 26782-71-8, D-tert-Leucine 28920-43-6, 9-Fluorenylmethyl chloroformate 28954-12-3, L-Allothreonine 29943-42-8, Tetrahydro-4H-pyran-4-one 30525-89-4, Paraformaldehyde 32366-02-2, N-Benzyl-N-methyl carbamoyl chloride 36024-28-9 37595-74-7, N-Phenyltriflimide 37736-82-6,

N-tert-Butoxycarbonyl-L-cyclohexylalanine 40299-87-4,
4-(Bromoacetyl)morpholine 41242-94-8, 2-Hydroxymethyl quinoxaline
52373-72-5 53333-76-9, 2,2-Dimethyl-1-propanesulfonyl chloride
58632-95-4, Boc-ON 59562-82-2 60456-21-5 67478-50-6 68835-89-2,
Di-tert-amyl dicarbonate 69739-34-0, tert-Butyldimethylsilyl triflate
76513-69-4, 2-(Trimethylsilyl)ethoxymethyl chloride 78879-20-6
80360-23-2 85613-64-5 86087-23-2, (S)-(+)-3-Hydroxytetrahydrofuran
106167-47-9 107202-43-7 112372-06-2, Furo[2,3-c]pyridine-2-
carboxaldehyde 127862-89-9 162537-72-6, Furo[2,3-c]pyridine-2-methanol
162537-73-7 162541-63-1 162678-30-0 162870-63-5
RL: RCT (Reactant)
(prepn. of aminediol-contg. peptide analogs as retroviral protease
inhibitors for treatment of HIV infection (AIDS))

IT 95-13-6P, 1H-Indene 102-14-7P 111-32-0P 272-62-8P,
Furo[3,2-b]pyridine 334-88-3P, Diazomethane 374-35-6P 558-43-0P
587-33-7P 815-17-8P 1184-93-6P 1191-31-7P 1615-14-1P,
1H-Imidazole-1-ethanol 1780-17-2P, 2-Quinolinemethanol 1796-25-4P
2215-63-6P 2258-42-6P, Acetic formic anhydride 2280-28-6P 2644-82-8P
2842-44-6P 2849-93-6P, 1H-Benzimidazole-2-carboxylic acid 3587-64-2P
3724-55-8P 4026-20-4P 4113-04-6P, 6-Quinolinecarboxaldehyde
4441-30-9P, 4-Morpholinepropanol 4647-42-1P 4647-43-2P 4754-27-2P
4856-97-7P, 1H-Benzimidazole-2-methanol 5105-78-2P 5367-24-8P
6970-72-5P 7467-35-8P 7525-64-6P 7748-36-9P, 3-Oxetanol
13737-35-4P 14477-66-8P 14598-96-0P 15546-08-4P 17450-34-9P
18096-68-9P, 1H-Indene-2-methanol 19458-29-8P 19539-50-5P,
Furo[2,3-c]pyridine 20120-24-5P 20361-09-5P 22892-29-1P
22929-52-8P 23249-97-0P, 1H-Benzimidazole-2-propanoic acid 24580-44-7P
24621-70-3P, 1H-Indole-2-methanol 25854-85-7P 25854-87-9P
30293-86-8P 31562-43-3P 33905-47-4P 34637-40-6P 35677-88-4P
37535-57-2P 37859-42-0P, 2-Benzothiazolemethanol 39497-64-8P
40594-83-0P 42417-65-2P 50411-26-2P 50531-59-4P 51110-97-5P,
2-Benzoxazolepropanol 53346-03-5P 56365-70-9P 57443-39-7P
59524-02-6P 60398-41-6P 60651-97-0P 62565-28-0P 62965-10-0P
64360-69-6P 66866-64-6P 67706-63-2P 70448-03-2P 73282-11-8P
77186-95-9P, 2-Benzoxazolemethanol 80466-51-9P 85328-36-5P
85951-09-3P 85995-53-5P 86096-65-3P 86562-71-2P 88246-12-2P
89464-59-5P 90819-30-0P 91968-72-8P 94882-74-3P 98737-29-2P
98760-08-8P 98955-64-7P 98997-01-4P 100516-88-9P,
6-Quinolinemethanol 100868-72-2P 102123-74-0P 102123-85-3P
102152-03-4P 102229-10-7P 102831-44-7P 104948-22-3P 106513-42-2P
108957-20-6P 112372-05-1P, Furo[3,2-b]pyridine-2-carboxaldehyde
113247-51-1P 113459-50-0P 114645-18-0P 115916-75-1P 127041-02-5P
127382-65-4P 128018-44-0P 131424-20-9P 134807-06-0P 134807-20-8P
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141978-97-4P 143372-45-6P 143372-46-7P 143372-47-8P 143576-95-8P
143688-65-7P 144186-00-5P 144186-52-7P 144825-44-5P 149357-61-9P
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162537-01-1P 162537-03-3P **162537-10-2P** 162537-11-3P
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162537-54-4P 162537-55-5P 162537-56-6P 162537-61-3P,
Furo[3,2-b]pyridine-2-methanol 162537-62-4P 162537-63-5P
162537-64-6P 162537-65-7P 162537-66-8P 162537-67-9P 162537-68-0P
162537-69-1P 162537-70-4P 162537-74-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of aminediol-contg. peptide analogs as retroviral protease inhibitors for treatment of HIV infection (AIDS))

IT 162538-06-9P 162538-07-0P 162538-09-2P 162538-16-1P 162538-17-2P
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162677-20-5P 162677-23-8P 162677-31-8P 162677-41-0P 162677-43-2P
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183256-04-4P 183256-05-5P 183256-06-6P 183256-07-7P 183256-08-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of aminediol-contg. peptide analogs as retroviral protease inhibitors for treatment of HIV infection (AIDS))

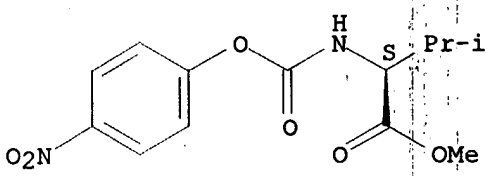
IT **162537-10-2P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of aminediol-contg. peptide analogs as retroviral protease inhibitors for treatment of HIV infection (AIDS))

RN 162537-10-2 HCAPLUS

CN L-Valine, N-[(4-nitrophenoxy)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L27 ANSWER 9 OF 24 HCAPLUS COPYRIGHT 2001 ACS

AN 1996:551382 HCAPLUS

DN 125:196378

TI Nitrogen mustard prodrugs with novel lipophilic protecting groups, and processes for their production

IN Springer, Caroline Joy; Niculescu-Duvaz, Ion

PA Cancer Research Campaign Technology Limited, UK

SO PCT Int. Appl., 44 pp.
CODEN: PIXXD2

DT Patent

LA English

IC ICM C07C275-32
ICS C07C271-54; C07C219-34; C07C271-28; A61K031-17; A61K031-27

CC 34-2 (**Amino Acids, Peptides,** and **Proteins**)
Section cross-reference(s): 1, 25, 63

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9622277	A1	19960725	WO 1996-GB112	19960119
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE				
	CA 2210347	AA	19960725	CA 1996-2210347	19960119
	AU 9644535	A1	19960807	AU 1996-44535	19960119
	AU 709251	B2	19990826		
	EP 804413	A1	19971105	EP 1996-900627	19960119
	EP 804413	B1	20000517		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
	JP 10512565	T2	19981202	JP 1996-522127	19960119
	AT 193012	E	20000615	AT 1996-900627	19960119
	ES 2149445	T3	20001101	ES 1996-900627	19960119
	US 6005002	A	19991221	US 1997-875099	19970716
PRAI	GB 1995-1052	A	19950119		
	WO 1996-GB112	W	19960119		

OS MARPAT 125:196378

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention provides compds. I and II [X, Y = Cl, Br, iodo, CH3SO3, or OSO2Ph (wherein Ph is optionally substituted by 1-5 alkyl, halo, cyano, and/or nitro); R1, R2 each = 1-4 optional substituents; Z1, Z2 = O, NH; R3 = H, t-Bu, allyl; Z3 = hydrocarbyl group such as carboxyethyl, optionally contg. heteroatoms] and their physiol. acceptable derivs. The compds. can be converted in situ into nitrogen mustard agents by the actions of enzymes such as carboxypeptidase or nitroreductase and are useful for the treatment of cancer (no data). For example, the glutamate ester L-Me3COCOCHRCH2CH2CO2CMe3 [III; R = NH2] was converted to the isocyanate III [R = NCO], which reacted with 4-hydroxybenzaldehyde to give 72% III [R = NHCO2C6H4CHO-4]. This was reduced with NaBH3CN to give 86% of III [R = NHCO2C6H4CH2OH-4], which was coupled with the nitrogen mustard 4-(OCN)C6H4N(CH2CH2Cl)2 in 90% yield, followed by deesterification with formic acid (87%), to give title compd. IV.

ST glutamate nitrogen mustard prodrug antitumor prepn

IT Neoplasm inhibitors
(prepn. of lipophilic glutamate-based nitrogen mustard prodrugs as anticancer agents)

IT Amino acids, preparation
Nitrogen mustards
RL: BAC (Biological activity or effector, except adverse); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of lipophilic glutamate-based nitrogen mustard prodrugs as anticancer agents)

IT Therapeutics
(pharmaco-, GDEPT (gene-directed enzyme prodrug therapy); prepn. of lipophilic glutamate-based nitrogen mustard prodrugs as anticancer agents)

IT Pharmaceutical dosage forms
(prodrugs, prepn. of lipophilic glutamate-based nitrogen mustard prodrugs as anticancer agents)

IT 9031-98-5, Carboxypeptidase 9037-41-6, Nitroreductase
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(activation by; prepn. of lipophilic glutamate-based nitrogen mustard prodrugs as anticancer agents)

IT 18483-99-3P, 4-Nitrobenzyl 2-tetrahydropyranyl ether 18484-05-4P, 4-Aminobenzyl 2-tetrahydropyranyl ether 113068-95-4P, 4-Isocyanatobenzyl tert-butyldiphenylsilyl ether 161803-03-8P, 4-Nitrobenzyl tert-butyldiphenylsilyl ether 161803-04-9P, 4-Aminobenzyl tert-butyldiphenylsilyl ether 161803-05-0P 161803-06-1P 180839-06-9P, 4-[N,N-Bis(2-chloroethyl)amino]phenyl trimethylsilyl ether 180839-08-1P 180839-11-6P 180839-12-7P 180839-13-8P 180839-14-9P 180839-15-0P 180839-16-1P 180839-17-2P 180839-18-3P 180839-19-4P **180839-20-7P 180839-21-8P** 180841-62-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(intermediate; prepn. of lipophilic glutamate-based nitrogen mustard prodrugs as anticancer agents)

IT 180838-97-5P 180839-00-3P 180839-02-5P 180839-04-7P
RL: BAC (Biological activity or effector, except adverse); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of lipophilic glutamate-based nitrogen mustard prodrugs as anticancer agents)

IT 180838-98-6P 180839-01-4P 180839-03-6P 180839-05-8P

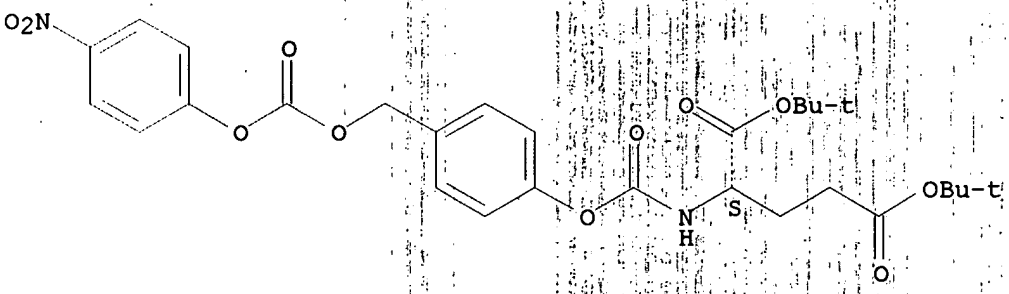
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of lipophilic glutamate-based nitrogen mustard prodrugs as anticancer agents)

IT 110-87-2 123-08-0, 4-Hydroxybenzaldehyde 619-73-8, 4-Nitrobenzyl alcohol 623-04-1, 4-Aminobenzyl alcohol 623-05-2, 4-Hydroxybenzyl alcohol 1204-69-9, 4-[N,N-Bis(2-chloroethyl)amino]phenol 7693-46-1, 4-Nitrophenyl chloroformate 20845-16-3 32677-01-3, Di-tert-butyl L-glutamate hydrochloride 57529-05-2, 4-(1,3-Dithian-2-yl)phenol 58479-61-1, tert-Butyldiphenylchlorosilane 82484-59-1, 4-[N,N-Bis(2-chloroethyl)amino]phenyl isocyanate
RL: RCT (Reactant)
(starting material; prepn. of lipophilic glutamate-based nitrogen mustard prodrugs as anticancer agents)

IT **180839-20-7P 180839-21-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(intermediate; prepn. of lipophilic glutamate-based nitrogen mustard prodrugs as anticancer agents)

RN 180839-20-7 HCAPLUS
CN L-Glutamic acid, N-[[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenoxy]carbonyl]-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

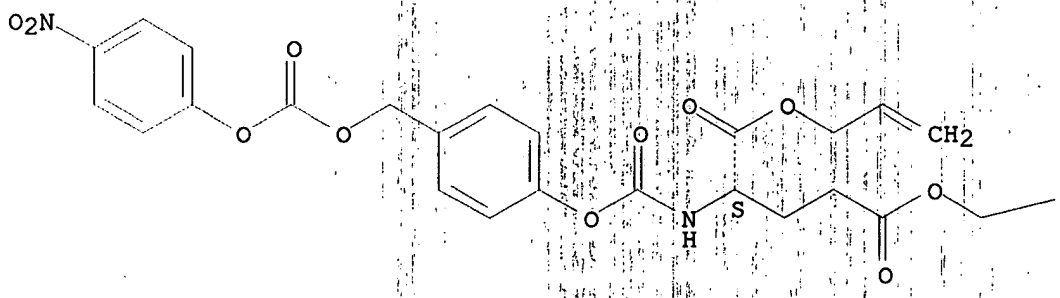
Absolute stereochemistry.

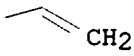


RN 180839-21-8 HCAPLUS
CN L-Glutamic acid, N-[[4-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]phenoxy]carbonyl]-, di-2-propenyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

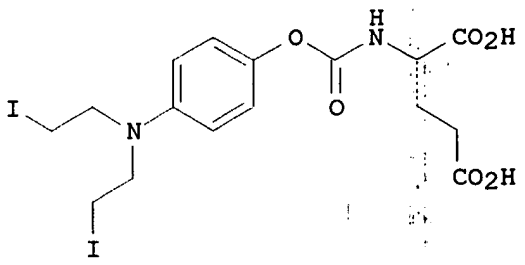




L27 ANSWER 10 OF 24 HCAPLUS COPYRIGHT 2001 ACS
AN 1996:509810 HCAPLUS
DN 125:168650
TI High-purity N-[4-[N,N-bis(2-iodoethyl)amino]phenoxycarbonyl]-L-glutamic acid and hydrogen iodide salt as prodrugs for ADEPT therapy
IN Heaton, David William; Dines, Susan; Dowell, Robert Ian
PA Zeneca Limited, UK
SO PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07C271-54
ICS A61K031-325
CC 34-2 (**Amino Acids, Peptides,** and **Proteins**)
Section cross-reference(s): 1, 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9620169	A1	19960704	WO 1995-GB2997	19951221
	W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	ZA 9510936	A	19960624	ZA 1995-10936	19951221
	CA 2204741	AA	19960704	CA 1995-2204741	19951221
	AU 9642700	A1	19960719	AU 1996-42700	19951221
	AU 702337	B2	19990218		
	GB 2309031	A1	19970716	GB 1997-8977	19951221
	GB 2309031	B2	19980812		
	EP 799193	A1	19971008	EP 1995-941219	19951221
	EP 799193	B1	20000816		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
	CN 1171100	A	19980121	CN 1995-196993	19951221
	HU 77288	A2	19980330	HU 1997-2207	19951221
	BR 9510463	A	19980609	BR 1995-10463	19951221
	AT 195511	E	20000915	AT 1995-941219	19951221
	FI 9702630	A	19970618	FI 1997-2630	19970618
	NO 9702883	A	19970620	NO 1997-2883	19970620
	US 5981791	A	19991109	US 1997-860880	19970623
PRAI	GB 1994-26133	A	19941223		
	WO 1995-GB2997	W	19951221		

OS MARPAT 125:168650
GI



AB A new salt of the prodrug N-[4-[N,N-bis(2-iodoethyl)amino]phenoxycarbonyl]-L-glutamic acid (I), which is useful in antibody directed enzyme prodrug therapy (ADEPT), is disclosed. This salt, the hydrogen iodide salt I.HI, is obtained in cryst. form with m.p. 142-145.degree. and has a specified X-ray powder diffraction spectrum. Prepn. of cryst. I.HI enables I to be prepd. in a highly pure form. I.HI also has advantages of good thermal stability, easy synthesis, and reduced hygroscopic/deliquescence properties. Improved stability may be due to reversal of degrdn. of the mustard alkylating arms of the mol. by HI. A multi-step prepn. of I from L-glutamic acid and p-O2NC6H4OCOCl is given. Mouse tumor xenograft expts. using therapy with F(ab')2A5B7-CPG2 conjugate (2.5 mg/kg i.v.) and I.HI (3 doses at 70 mg/kg i.p. each) gave tumor regression and >30 day growth delays with only minor effects on body wt. and peripheral white blood cell counts.

ST iodoethylaminophenoxycarbonylglutamic acid hydriodide antitumor prodrug ADEPT; bisiodoethylaminophenoxycarbonylglutamic acid prepn antitumor prodrug ADEPT

IT Neoplasm inhibitors
(prepn. of high-purity [[bis(iodoethyl)amino]phenoxycarbonyl]glutamic acid and hydriodide salt as antitumor prodrugs for ADEPT)

IT Pharmaceutical dosage forms
(prodrugs, antibody-directed enzyme prodrug therapy (ADEPT); prepn. of high-purity [[bis(iodoethyl)amino]phenoxycarbonyl]glutamic acid and hydriodide salt as antitumor prodrugs for ADEPT)

IT Pharmaceutical dosage forms
(prodrugs, prepn. of high-purity [[bis(iodoethyl)amino]phenoxycarbonyl] glutamic acid and hydriodide salt as antitumor prodrugs for ADEPT)

IT 5269-43-2P, L-Glutamic acid bis(trimethylsilyl) ester **156079-00-4P**
156079-01-5P 156079-89-9P 172974-17-3P 180031-70-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(intermediate; prepn. of high-purity [[bis(iodoethyl)amino]phenoxycarbo nyl]glutamic acid and hydriodide salt as antitumor prodrugs for ADEPT)

IT 180031-69-0P
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); IMF (Industrial manufacture); PRP (Properties); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of high-purity [[bis(iodoethyl)amino]phenoxycarbonyl]glutamic acid and hydriodide salt as antitumor prodrugs for ADEPT)

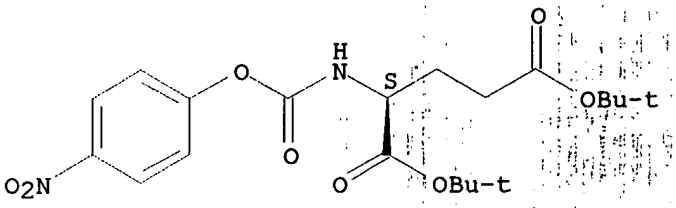
IT 156079-88-8P
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); IMF (Industrial manufacture); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of high-purity [[bis(iodoethyl)amino]phenoxycarbonyl]glutamic acid and hydriodide salt as antitumor prodrugs for ADEPT)

IT 56-86-0, L-Glutamic acid, reactions 75-21-8, Ethylene oxide, reactions 75-77-4, Chlorotrimethylsilane, reactions 115-11-7, Isobutylene, reactions 7693-46-1, p-Nitrophenyl chloroformate
RL: RCT (Reactant)
(starting material; prepn. of high-purity [[bis(iodoethyl)amino]phenoxy carbonyl]glutamic acid and hydriodide salt as antitumor prodrugs for ADEPT)

IT **156079-00-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(intermediate; prepn. of high-purity [[bis(iodoethyl)amino]phenoxycarbonyl]glutamic acid and hydriodide salt as antitumor prodrugs for ADEPT)

RN 156079-00-4 HCAPLUS
CN L-Glutamic acid, N-[(4-nitrophenoxy)carbonyl]-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

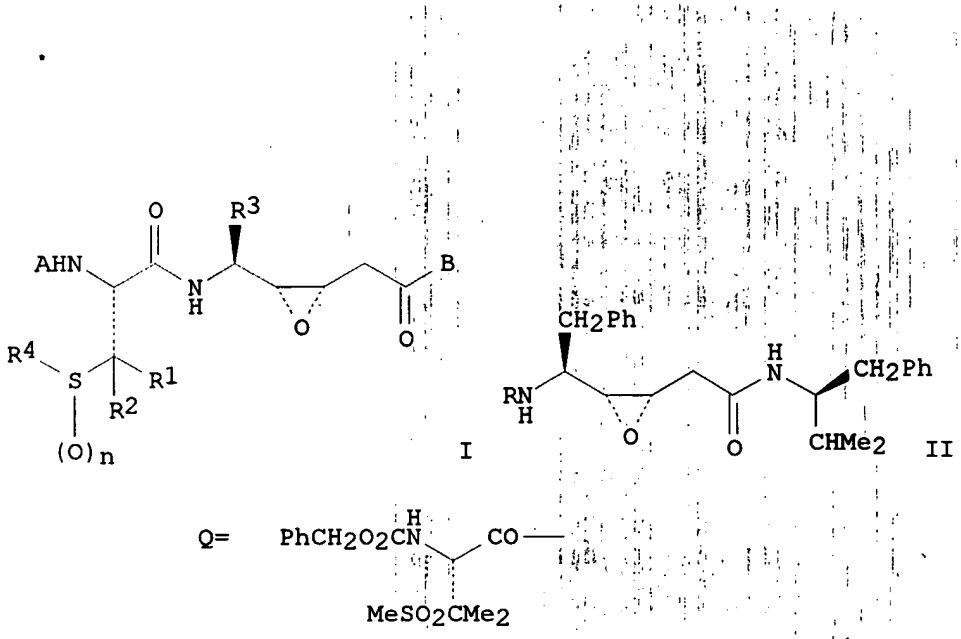
Absolute stereochemistry.



L27 ANSWER 11 OF 24 HCAPLUS COPYRIGHT 2001 ACS
AN 1996:171803 HCAPLUS
DN 124:233139
TI Preparation of sulfonylamino acid amides containing cis-epoxide as irreversible HIV protease inhibitors
IN Yoon, Heungsik; Choy, Nakyen; Kim, Sung Chun; Choi, Ho Il; Son, Young Chan; Park, Chi Hyo; Moon, Kwang-Yul; Jung, Wonhee; Kim, Chung Ryeol; et al.
PA IG Chemical Ltd., S. Korea
SO Eur. Pat. Appl., 58 pp.
CODEN: EPXXDW
DT Patent
LA English
IC ICM C07D303-36
ICS C07D303-40; C07D405-12; C07D407-12; A61K031-335; A61K031-435
CC 34-2 (**Amino Acids, Peptides,** and **Proteins**)
Section cross-reference(s): 1
FAN.CNT 7

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 687675	A2	19951220	EP 1995-108908	19950609
EP 687675	A3	19960306		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
KR 125117	B1	19971205	KR 1994-13423	19940615
JP 08193077	A2	19960730	JP 1995-172733	19950615
JP 2987313	B2	19991206		
PRAI KR 1994-13423	A	19940615		

OS MARPAT 124:233139
GI



AB Novel cis-epoxide compds. [I; R1, R2 = H, alkyl; R3 = (un)substituted aryl or alkyl; R4 = H, C1-4 alkyl; n = 0,1,2; A = (X)(Y)mR5, NR6R7, ZCHR8R9; wherein X = CO, COCO, CO, SO2, CS; Y = O, CH2, NH, NMe; m = 0,1; R5 = heterocyclyl, straight or branched or cyclic C1-8 alkyl or alkoxy, heterocyclylalkyl, cycloalkylalkyl, arylalkoxy; R6 = straight or branched C1-8 alkyl, cycloalkyl, cycloalkylalkyl; R7 = H, alkyl; Z = O, NH, NMe; R8, R9 = alkyl optionally substituted by arom. hydrocarbyl or cycloalkyl, C3-8 cycloalkyl, aryl], useful for treating or preventing diseases caused by HIV infection, are prepd. The novel HIV protease inhibitor I has a specific structure to form a stable bonding with the enzyme active site, which entails a highly enhanced irreversible inhibition against HIV protease. An anti-AIDS or immunomodulator contains a therapeutically effective amt. of said cis-epoxide I. Thus, (S)-5-[(N-benzyloxycarbonyl)amino]-6-phenyl-(cis)-3-hexene-1-carboxylic acid was condensed with (S)-2-amino-3-methyl-1-phenylbutane using N-ethyl-N'-(3-(dimethylamino)propyl)carbodiimide hydrochloride (EDC) and HOBT in DMF followed by epoxidn. with m-chloroperbenzoic acid in CH2Cl2 to give the cis-epoxide (II; R = PhCH2O2C), which was hydrogenolyzed in the presence of 10% Pd-C in MeOH under an atm. of H, coupled with N-benzyloxycarbonyl-.beta.-(S-methyl)-L-valine using EDC and HOBT in DMF , and oxidized with m-chloroperbenzoic acid in CH2Cl2 to give the title compd. II (R = Q). The latter compd. in vitro inhibited HIV protease with the inhibition const. Kina/Ki min-1M-1 109-1010 (Kina = a rate const. indicating rate of chem. reaction forming covalent bond between an enzyme and an inhibitor in Michaelis-Menten complex; Ki = an inhibition const. indicating the dissocn. rate of Michaelis-Menten complex into an enzyme and an inhibitor) and in vitro showed IC50 of 1 nM for inhibiting the HIV-1 infection of H9 or Sup T1 cell lines.

ST cis epoxide prepn HIV protease inhibitor; irreversible HIV protease inhibitor; sulfonylamino acid amide contg cis epoxide

IT Acquired immune deficiency syndrome
Virucides and Virustats
(prepn. of sulfonylamino acid amides contg. cis-epoxide as irreversible HIV protease inhibitors for treating AIDS)

IT Amides, preparation
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino, prepn. of sulfonylamino acid amides contg. cis-epoxide as irreversible HIV protease inhibitors for treating AIDS)

IT Epoxides
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic

preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cis-, prepn. of sulfonylamino acid amides contg. cis-epoxide as irreversible HIV protease inhibitors for treating AIDS)

IT Virus, animal
(human immunodeficiency 1, prepn. of sulfonylamino acid amides contg. cis-epoxide as irreversible HIV protease inhibitors for treating AIDS)

IT 174562-29-9P 174562-30-2P 174562-31-3P 174562-32-4P 174562-33-5P
174562-34-6P 174562-35-7P 174562-36-8P 174562-37-9P 174562-38-0P
174562-39-1P 174562-40-4P 174562-41-5P 174562-42-6P 174562-43-7P
174562-44-8P 174562-45-9P 174562-46-0P 174562-47-1P 174562-48-2P
174562-49-3P 174562-50-6P 174562-51-7P 174562-52-8P 174562-53-9P
174562-54-0P 174562-55-1P 174562-56-2P 174562-57-3P 174562-58-4P
174562-59-5P 174562-60-8P 174562-61-9P 174562-62-0P 174562-63-1P
174562-64-2P 174562-65-3P 174562-66-4P 174562-67-5P 174562-68-6P
174562-69-7P 174562-70-0P 174562-71-1P 174562-72-2P 174562-73-3P
174562-74-4P 174562-75-5P 174562-76-6P 174562-77-7P 174562-78-8P
174562-79-9P 174562-80-2P 174562-81-3P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of sulfonylamino acid amides contg. cis-epoxide as irreversible HIV protease inhibitors for treating AIDS)

IT 144114-21-6, Retropepsin
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(prepn. of sulfonylamino acid amides contg. cis-epoxide as irreversible HIV protease inhibitors for treating AIDS)

IT 59-67-6, 3-Pyridinecarboxylic acid, reactions 74-88-4, Iodomethane, reactions 78-77-3, Isobutyl bromide 78-82-0, Isobutyronitrile 88-14-2, 2-Furancarboxylic acid 96-41-3, Cyclopentyl alcohol 98-00-0, 2-Furanmethanol 98-59-9, Toluenesulfonyl chloride 98-98-6, 2-Pyridinecarboxylic acid 100-39-0, Benzyl bromide 100-46-9, Benzylamine, reactions 100-55-0, 3-Pyridylcarbinol 110-68-9, Methyl-N-butylamine 501-53-1, Benzyl chloroformate 503-74-2, Isovaleric acid 527-72-0, 2-Thiophenic acid 574-98-1, N-(2-Bromoethyl)phthalimide 586-95-8, 4-Pyridylcarbinol 586-98-1, 2-Pyridylcarbinol 603-35-0, Triphenylphosphine, reactions 617-89-0, 2-Furanylmethylamine 625-45-6, Methoxyacetic acid 1113-41-3, L-Penicillamine 1779-49-3, Methyltriphenylphosphonium bromide 2516-33-8, Cyclopropylmethanol 2516-47-4, Cyclopropylmethylamine 4083-57-2, 3-Amino-2,4-dimethylpentane 6921-34-2, Benzylmagnesium chloride 7693-46-1, p-Nitrophenyl chloroformate 13734-34-4 23844-66-8, (R)-1-Amino-2-methyl-1-phenylpropane 24424-99-5, Di-tert-Butyl dicarbonate 24939-24-0, p-Aminobenzenesulfonyl chloride 33445-07-7, Isopropoxyacetic acid 37222-66-5, Oxone 59830-60-3, N-Benzyloxycarbonyl-L-phenylalaninal 68906-26-3, (S)-1-Amino-2-methyl-1-phenylpropane 69492-74-6, Thiopheneacetic acid 74124-79-1, Disuccinimidyl carbonate 96928-87-9 111491-96-4 137867-58-4, Furanacetic acid 174562-82-4
RL: RCT (Reactant)
(prepn. of sulfonylamino acid amides contg. cis-epoxide as irreversible HIV protease inhibitors for treating AIDS)

IT 65273-64-5P 82894-53-9P 97589-56-5P 100217-05-8P 112898-22-3P
156641-79-1P 156641-80-4P 156641-81-5P 156641-82-6P 156641-83-7P
156715-06-9P 160742-44-9P 160742-45-0P 174562-83-5P 174562-84-6P
174562-85-7P 174562-86-8P 174562-87-9P 174562-88-0P 174562-89-1P
174562-90-4P **174562-91-5P** 174562-92-6P 174562-93-7P
174562-94-8P 174689-86-2P 174689-87-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of sulfonylamino acid amides contg. cis-epoxide as irreversible

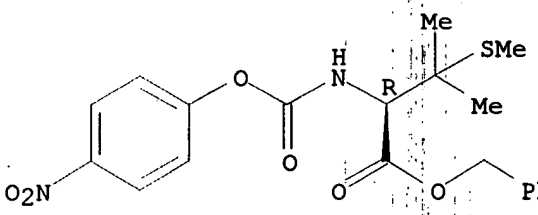
HIV protease inhibitors for treating AIDS)

IT **174562-91-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of sulfonylamino acid amides contg. cis-epoxide as irreversible HIV protease inhibitors for treating AIDS)

RN 174562-91-5 HCAPLUS

CN L-Valine, 3-(methylthio)-N-[(4-nitrophenoxy)carbonyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L27 ANSWER 12 OF 24 HCAPLUS COPYRIGHT 2001 ACS

AN 1995:994162 HCAPLUS

DN 124:87790

TI Pharmaceutical compositions containing HIV protease inhibitors and their preparation.

IN Al-Razzak, Laman; Marsh, Kennan C.; Manning, Lourdes P.; Kaul, Dilip

PA Abbott Laboratories, USA

SO PCT Int. Appl., 58 pp.
CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K031-425
ICS A61K009-08; A61K047-10; A61K047-12; A61K047-14

CC 34-2 (**Amino Acids, Peptides,** and **Proteins**)
Section cross-reference(s): 63

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9520384	A1	19950803	WO 1995-US232	19950103
	W: AU, CA, JP, KR, MX				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	IL 111991	A1	20000726	IL 1994-111991	19941215
	CA 2178632	AA	19950803	CA 1995-2178632	19950103
	AU 9515248	A1	19950815	AU 1995-15248	19950103
	AU 700942	B2	19990114		
	EP 732923	A1	19960925	EP 1995-906790	19950103
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	JP 09508383	T2	19970826	JP 1995-520059	19950103
	US 5484801	A	19960116	US 1995-440277	19950512
PRAI	US 1994-189021	A	19940128		
	US 1994-283239	A	19940729		
	WO 1995-US232	W	19950103		

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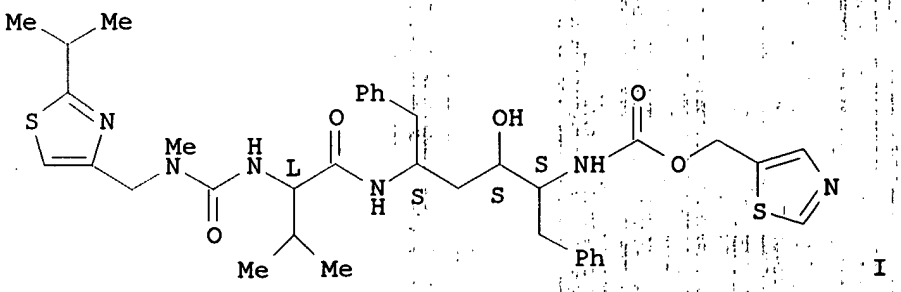


I

AB A pharmaceutical compn. which comprises a soln. of an HIV protease inhibiting compd. (e.g., I) in a pharmaceutically acceptable org. solvent comprising a mixt. of (1): (a) a solvent selected from propylene glycol and polyethylene glycol or (b) a solvent selected from polyoxyethyleneglycerol triricinoleate, polyethylene glycol 40 hydrogenated castor oil, fractioned coconut oil, polyoxyethylene 20 sorbitan monooleate and 2-(2-ethoxyethoxy)ethanol or (c) a mixt. thereof; and (2) ethanol or propylene glycol, is claimed. I was prepd. in many steps and its bioavailability in various formulations was studied.

ST hiv protease inhibitor pharmaceutical compn; valinyldiphenylhexane prepn hiv protease inhibitor

IT Pharmaceutical dosage forms
(pharmaceutical compns. contg. HIV protease inhibitors and their prepn.)

IT 155213-67-5P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(pharmaceutical compns. contg. HIV protease inhibitors and their prepn.)

IT 143838-10-2P 144164-10-3P
RL: BYP (Byproduct); PREP (Preparation)
(pharmaceutical compns. contg. HIV protease inhibitors and their prepn.)

IT 62-56-6, Thiourea, reactions 75-12-7, Formamide, reactions 105-39-5, Ethyl chloroacetate 109-94-4, Ethyl formate 534-07-6, 1,3-Dichloroacetone 563-83-7, Isobutyramide 4070-48-8, Valine methyl ester 6372-14-1, N-Benzyloxycarbonylphenylalaninol 40635-67-4, .alpha.-Acetoxyisobutyryl bromide 156732-13-7 156732-15-9
RL: RCT (Reactant)
(pharmaceutical compns. contg. HIV protease inhibitors and their prepn.)

IT 115-08-2P, Thioformamide 13515-65-6P 32955-21-8P, 2-Amino-5-(ethoxycarbonyl)thiazole 32955-22-9P, Ethyl thiazole-5-carboxylate 33142-21-1P, Ethyl 2-chloro-2-formylacetate 38585-74-9P, 5-Hydroxymethylthiazole 59830-60-3P 65386-28-9P 137649-69-5P 144141-68-4P 144163-44-0P 144163-85-9P 144163-97-3P 144164-11-4P 154212-59-6P 154212-60-9P 154212-61-0P 154248-99-4P **162537-10-2P** 162849-92-5P 162849-93-6P 162849-94-7P 162849-95-8P 162849-96-9P, 2-Amino-5-(ethoxycarbonyl)thiazole hydrochloride 162990-03-6P 165315-39-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(pharmaceutical compns. contg. HIV protease inhibitors and their prepn.)

IT 162990-01-4
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. contg. HIV protease inhibitors and their

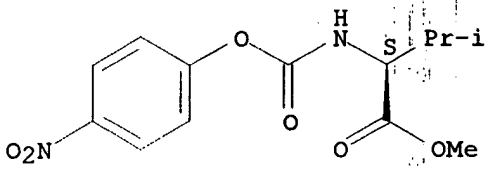
prepn.)

IT **162537-10-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(pharmaceutical compns. contg. HIV protease inhibitors and their prepn.)

RN 162537-10-2 HCAPLUS

CN L-Valine, N-[(4-nitrophenoxy)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L27 ANSWER 13 OF 24 HCAPLUS COPYRIGHT 2001 ACS

AN 1995:965043 HCAPLUS

DN 124:117909

TI Optimization of Alkylating Agent Prodrugs Derived from Phenol and Aniline Mustards: A New Clinical Candidate Prodrug (ZD2767) for Antibody-Directed Enzyme Prodrug Therapy

AU Springer, Caroline J.; Dowell, Robert; Burke, Philip J.; Hadley, Elma; Davies, D. Huw; Blakey, David C.; Melton, Roger G.; Niculescu-Duvaz, Ion

CS Cancer Research Campaign Centre for Cancer Therapeutics, Institute of Cancer Research, Sutton, SM2 5NG, UK

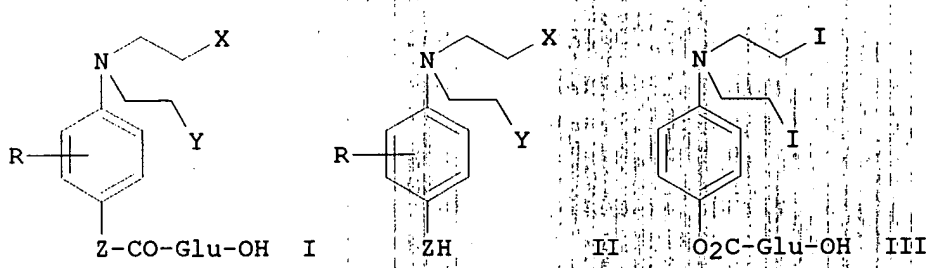
SO J. Med. Chem. (1995), 38(26), 5051-65
CODEN: JMCMAR; ISSN: 0022-2623

DT Journal

LA English

CC 34-2 (**Amino Acids, Peptides,** and **Proteins**)
Section cross-reference(s): 1

GI



AB Sixteen novel potential prodrugs I [R = H, 2-Me, 2-Cl, 3-Me, 3-Me2CH, 3-F, 2,3-(CH:CHCH:CH), 3-CN; Z = O, NH; X, Y = Cl, Br, iodo, O3SMe] derived from phenol or aniline mustards and their 16 corresponding drugs II with ring substitution and/or different alkylating functionalities were designed. They are bifunctional alkylating agents in which the activating effect of the phenolic hydroxyl or amino function is masked through an oxycarbonyl or a carbamoyl bond to a glutamic acid. These prodrugs were

designed to be activated to their corresponding phenol and aniline nitrogen mustard drugs at a tumor site by prior administration of a monoclonal antibody conjugated to the bacterial enzyme carboxypeptidase G2 (CPG2) in antibody-directed enzyme prodrug therapy (ADEPT). The synthesis of the analogous novel parent drugs II is also described. The viability of a colorectal cell line (LoVo) was monitored with the potential prodrugs and the parent drugs. The differential in the cytotoxicity between the potential prodrugs and their corresponding active drugs ranged between 12 and >195 fold. Some compds. I exhibited substantial prodrug activity, since a cytotoxicity differential of >100 was achieved compared to the analogous II. The ability of the potential prodrugs to act as substrates for CPG2 was detd. (kinetic parameters KM and kcat), and the chem. stability was measured for all the compds. The unsubstituted phenols with different alkylating functionalities (I; R = H, Z = O) proved to have the highest ratio of substrates kcat:KM. From these studies, III (ZD2767) emerges as a new ADEPT clin. trial candidate due to its physicochem. and biol. characteristics.

ST ZD 2767 prepn biol alkylating agent; glutamate aniline mustard prepn ADEPT; phenol glutamate mustard prepn ADEPT; structure activity alkylating agent prodrug

IT Neoplasm inhibitors
(optimization of alkylating agent prodrugs derived from phenol and aniline mustards in prepn. of prodrug ZD2767 for antibody-directed enzyme prodrug therapy)

IT Alkylating agents, biological
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(optimization of alkylating agent prodrugs derived from phenol and aniline mustards in prepn. of prodrug ZD2767 for antibody-directed enzyme prodrug therapy)

IT Antibodies
Enzymes
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(optimization of alkylating agent prodrugs derived from phenol and aniline mustards in prepn. of prodrug ZD2767 for antibody-directed enzyme prodrug therapy)

IT Molecular structure-biological activity relationship
(cytotoxic, optimization of alkylating agent prodrugs derived from phenol and aniline mustards in prepn. of prodrug ZD2767 for antibody-directed enzyme prodrug therapy)

IT Pharmaceutical dosage forms
(prodrugs, optimization of alkylating agent prodrugs derived from phenol and aniline mustards in prepn. of prodrug ZD2767 for antibody-directed enzyme prodrug therapy)

IT 21667-05-0P 156078-84-1P 156079-29-7P 156079-30-0P 156079-31-1P
156079-32-2P 156079-34-4P 156079-35-5P 172974-00-4P 172974-01-5P
172974-02-6P 172974-03-7P 172974-19-5P 172974-20-8P 172974-21-9P
172974-22-0P
RL: BAC (Biological activity or effector, except adverse); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(optimization of alkylating agent prodrugs derived from phenol and aniline mustards in prepn. of prodrug ZD2767 for antibody-directed enzyme prodrug therapy)

IT 156078-82-9P 156078-91-0P 156078-94-3P 156078-98-7P 156079-02-6P
156079-03-7P 156079-04-8P 156079-05-9P 156079-06-0P 156079-07-1P
156079-56-0P 156079-57-1P 156079-88-8P, ZD 2767 156079-91-3P
172974-23-1P 172974-24-2P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(optimization of alkylating agent prodrugs derived from phenol and

aniline mustards in prepn. of prodrug ZD2767 for antibody-directed enzyme prodrug therapy)

IT 75-21-8, Oxirane, reactions 111-42-2, reactions 350-30-1, 3-Chloro-4-fluoronitrobenzene 369-34-6, 3,4-Difluoronitrobenzene 399-96-2, 4-Amino-2-fluorophenol 2791-84-6 2834-90-4, 4-Amino-1-naphthol 2835-96-3, 4-Amino-2-methylphenol 2835-99-6, 4-Amino-3-methylphenol 3964-52-1, 4-Amino-2-chlorophenol 5854-73-9 7693-46-1, 4-Nitrophenyl chloroformate 17417-09-3, 2-Fluoro-5-nitrobenzonitrile 17609-80-2, 4-Amino-3-chlorophenol 32677-01-3, Di-tert-butyl glutamate hydrochloride 82774-61-6 156639-14-4 172974-26-4
RL: RCT (Reactant)
(optimization of alkylating agent prodrugs derived from phenol and aniline mustards in prepn. of prodrug ZD2767 for antibody-directed enzyme prodrug therapy)

IT 65976-57-0P 65976-66-1P 156078-83-0P 156078-85-2P 156078-86-3P
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156079-00-4P 156079-01-5P 156079-08-2P 156079-09-3P
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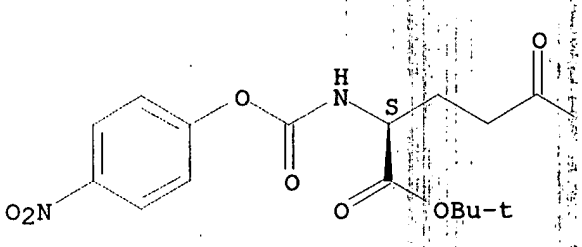
172974-16-2P 172974-17-3P 172974-18-4P 172974-25-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(optimization of alkylating agent prodrugs derived from phenol and aniline mustards in prepn. of prodrug ZD2767 for antibody-directed enzyme prodrug therapy)

IT **156079-00-4P 172974-16-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(optimization of alkylating agent prodrugs derived from phenol and aniline mustards in prepn. of prodrug ZD2767 for antibody-directed enzyme prodrug therapy)

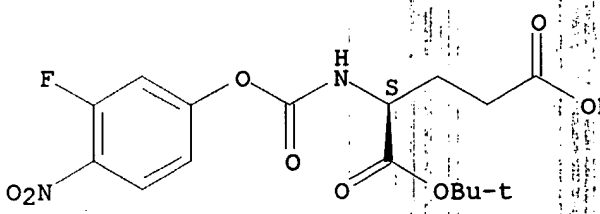
RN 156079-00-4 HCAPLUS
CN L-Glutamic acid, N-[(4-nitrophenoxy)carbonyl]-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 172974-16-2 HCAPLUS
CN L-Glutamic acid, N-[(3-fluoro-4-nitrophenoxy)carbonyl]-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L27 ANSWER 14 OF 24 HCAPLUS COPYRIGHT 2001 ACS
AN 1995:958521 HCAPLUS
DN 124:176946
TI Preparation of retroviral protease inhibiting peptide analogs.
IN Norbeck, Daniel W.; Sham, Hing L.; Kempf, Dale J.; Zhao, Chen
PA Abbott Laboratories, USA
SO U.S., 66 pp. Cont.-in-part of U.S. Ser. No. 23,226, abandoned.
CODEN: USXXAM
DT Patent
LA English
IC ICM A61K031-44
ICS A61K031-425; A61K031-42; C07D413-14; C07D417-14; C07D263-30; C07D277-20
NCL 514333000
CC 34-3 (**Amino Acids, Peptides, and Proteins**)
Section cross-reference(s): 1

FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 5461067	A	19951024	US 1994-185666	19940201
WO 9419332	A1	19940901	WO 1994-US1457	19940208
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2155338	AA	19940901	CA 1994-2155338	19940208
EP 683772	A1	19951129	EP 1994-908018	19940208
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
JP 08507061	T2	19960730	JP 1994-519025	19940208
US 5621109	A	19970415	US 1995-455922	19950531
US 5631376	A	19970520	US 1995-455458	19950531
US 5990135	A	19991123	US 1995-455052	19950531
PRAI US 1993-23226		19930225		
US 1994-185666		19940201		
WO 1994-US1457		19940208		

OS MARPAT 124:176946
AB R6YmNHCHR1CH(OH)CH2NR2NH(Y1)nR5 [R1, R2 = H, alkyl, aryl, thioalkoxyalkyl, aralkyl, cycloalkyl, guanidinoalkyl, arylthioalkoxyalkyl, cycloalkyloxyalkyl, cycloalkylsulfonylalkyl, aminocarbonylalkyl, etc.; Y = NHCHR4CO, NHNR4CO, etc.; Y1 = COCHR3NH, CONR3NH, etc.; R5, R6 = C(:T)GR7; T = O, S; G = CH2, O, S, NR8; R8 = H, alkyl, cycloalkyl; R7 = alkyl, cycloalkyl, aryl, arylalkyl, arylalkoxyalkyl, aminoalkyl, N-protected aminoalkyl, alkylaminoalkyl, N-protected alkylaminoalkyl, dialkylaminoalkyl, carboxyalkoxyalkyl, (alkoxycarbonyl)alkoxyalkyl, carboxyalkyl, alkoxycarbonylalkyl, aminocarboxyalkyl, N-protected aminocarboxyalkyl, alkylaminocarboxyalkyl, etc.; m, n = 0, 1], were prepd. Thus, (5S)-[[(5-thiazolyl)methoxy]carbonyl]amino-2-[(N-2-oxazolyl)methoxycarbonyl]amino-4S-hydroxy-1-(3-furanyl)-6-phenyl-2-azahexane (soln. phase prepn. given) inhibited HIV-13B in MT4 cells with IC50 = 0.029-0.032 .mu.M.
ST peptide analog prepn retroviral protease inhibitor; aminopropylhydrazine

azolylmethoxycarbonyl amino acid prepn virucide

IT Virucides and Virustats
(prepn. of retroviral protease inhibiting peptide analogs)

IT Peptides, preparation
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(analogs, prepn. of retroviral protease inhibiting peptide analogs)

IT Virus, animal
(human immunodeficiency 1, treatment of HIV infections; prepn. of retroviral protease inhibiting peptide analogs)

IT 144114-21-6, Retropepsin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(HIV protease inhibitors; prepn. of retroviral protease inhibiting peptide analogs)

IT 150767-06-9P 150767-07-0P 162739-20-0P 162739-21-1P 162739-22-2P
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RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of retroviral protease inhibiting peptide analogs)

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RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of retroviral protease inhibiting peptide analogs)

IT 173771-65-8P 173771-66-9P 173771-67-0P 173771-68-1P 173771-69-2P
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RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of retroviral protease inhibiting peptide analogs)

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RL: RCT (Reactant)
(prepn. of retroviral protease inhibiting peptide analogs)

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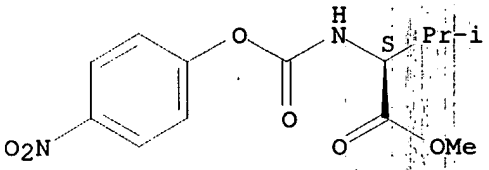
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of retroviral protease inhibiting peptide analogs)

IT **162537-10-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of retroviral protease inhibiting peptide analogs)

RN 162537-10-2 HCAPLUS

CN L-Valine, N-[(4-nitrophenoxy)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L27 ANSWER 15 OF 24 HCAPLUS COPYRIGHT 2001 ACS

AN 1995:695866 HCAPLUS

DN 123:84005

TI Preparation of peptide analogs as retroviral protease inhibitors.

IN Kempf, Dale J.; Norbeck, Daniel W.; Sham, Hing Leung; Zhao, Chen; Sowin, Thomas J.; Reno, Daniel S.; Haight, Anthony R.; Cooper, Arthur J.

PA Abbott Laboratories, USA

SO PCT Int. Appl., 194 pp.
CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K031-425
ICS A61K031-42; C07D277-24; C07D275-02; C07D261-08; C07D263-32

CC 34-3 (**Amino Acids, Peptides,** and **Proteins**)
Section cross-reference(s): 1

FAN.CNT 6

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9414436	A1	19940707	WO 1993-US12326	19931216
W: AU, CA, JP, KR				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
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CA 2135890	AA	19940707	CA 1993-2135890	19931216
CA 2135890	C	19960827		
AU 9459546	A1	19940719	AU 1994-59546	19931216
AU 659575	B2	19950518		
EP 674513	A1	19951004	EP 1994-905429	19931216
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	EP 727419	A3	19961030		
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	EP 1090914	A3	20010418		
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	IL 108126	A1	19950330	IL 1993-108126	19931221
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	US 5591860	A	19970107	US 1995-416272	19950404
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	EP 1996-106301	A3	19931216		
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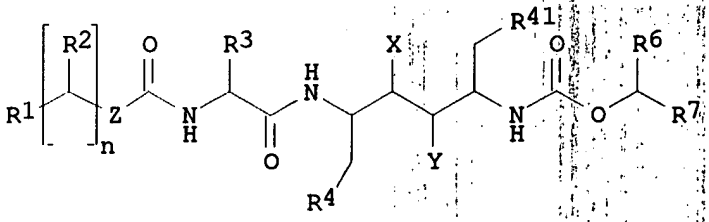
	US 1995-417879	A3	19950406		
	US 1995-418031	A3	19950406		
OS	MARPAT 123:84005				

GI



I

AB Title compds. [I; R1 = monosubstituted thiazolyl, oxazolyl, isoxazolyl, isothiazolyl; n = 1-3; R2, R6 = H, alkyl; R3 = alkyl; R4, R41 = (substituted) Ph, thiazolyl, oxazolyl; R7 = (alkyl-substituted) thiazolyl, oxazolyl, isoxazolyl, isothiazolyl; X = H, Y = OH, or X = OH, Y = H; Z = null, O, S, CH2, NR8; R8 = alkyl, cycloalkyl, OH, NH2, etc.; with provisos], were prepd. Thus, (2S,3S,5S)-5-[N-[N-[[N-methyl-N-[(2-isopropyl-4-thiazolyl)methyl]amino]carbonyl]valinyl]amino]-2-[N-[(5-thiazolyl)methoxycarbonyl]amino]-1,6-diphenyl-3-hydroxyhexane (prepn. via dimerization of Z-phenylalaninal given) inhibited HIV-13B in MT4 cells with IC50 = 0.025-0.040 .mu.M.

ST peptide analog prepn hiv protease inhibitor; virucide heterocyclylpeptide analog

IT Virucides and Virustats
(prepn. of peptide analogs as retroviral protease inhibitors)

IT Peptides, preparation
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of peptide analogs as retroviral protease inhibitors)

IT Virus, animal
(human immunodeficiency, infection; prepn. of peptide analogs as retroviral protease inhibitors)

IT 155213-67-5P 165314-93-2P 165314-94-3P 165314-95-4P 165314-96-5P
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165315-02-6P 165315-03-7P 165315-04-8P 165315-05-9P 165315-06-0P
165315-07-1P 165315-08-2P 165315-09-3P 165315-10-6P 165315-11-7P
165315-12-8P 165315-13-9P 165315-14-0P 165315-15-1P 165315-16-2P
165315-17-3P 165315-18-4P 165315-19-5P 165315-20-8P 165315-21-9P
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165315-27-5P 165315-28-6P 165315-29-7P 165315-30-0P 165315-31-1P
165315-32-2P 165315-33-3P 165315-34-4P 165315-35-5P 165315-36-6P
165315-37-7P 165315-38-8P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of peptide analogs as retroviral protease inhibitors)

IT 144114-21-6, Retropepsin
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(prepn. of peptide analogs as retroviral protease inhibitors)

IT 60-35-5, Acetamide, reactions 62-55-5, Thioacetamide 62-56-6, Thiourea, reactions 63-91-2, Phenylalanine, reactions 70-23-5, Ethyl bromopyruvate 74-89-5, Methylamine, reactions 75-04-7, Ethanamine, reactions 75-05-8, Acetonitrile, reactions 75-12-7, Formamide, reactions 75-44-5, Carbonic dichloride 78-81-9, Isobutylamine 79-05-0, Propionamide 88-09-5, 2-Ethylbutyric acid 105-39-5, Ethyl chloroacetate 107-10-8, 1-Aminopropane, reactions 109-89-7, reactions

110-91-8, Morpholine, reactions 122-51-0 123-39-7, N-Methylformamide
123-75-1, Pyrrolidine, reactions 503-74-2, 3-Methylbutyric acid
534-07-6, 1,3-Dichloroacetone 539-74-2, Ethyl 3-bromopropionate
563-83-7, Isobutyramide 638-07-3, Ethyl 4-chloroacetoacetate 867-13-0
870-46-2, tert-Butyl carbazate 1118-02-1, Trimethylsilyl isocyanate
1759-53-1, Cyclopropanecarboxylic acid 2491-20-5, Alanine methyl ester
hydrochloride 3400-45-1, Cyclopentanecarboxylic acid 3721-95-7,
Cyclobutanecarboxylic acid 5470-11-1 6065-82-3, Ethyl diethoxyacetate
6089-04-9 6160-65-2, Thiocarbonyl diimidazole 6306-52-1, Valine methyl
ester hydrochloride 6372-14-1, Z-Phenylalaninol 6921-34-2,
Benzylmagnesium chloride 6972-05-0, N,N-Dimethylthiourea 7204-46-8,
N,N-Diethylthiourea 13734-41-3 16332-06-2 16982-21-1, Ethyl
thiooxamate 19967-55-6 38585-74-9, 5-Thiazolemethanol 65386-28-9
65815-64-7 131052-44-3 133047-44-6 154212-61-0 162739-63-1
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RL: RCT (Reactant)
(prepn. of peptide analogs as retroviral protease inhibitors)

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Propanethioamide 1114-38-1P 1503-98-6P, Cyclobutanecarboxamide
3217-94-5P, Cyclopentanecarboxamide 6228-73-5P, Cyclopropanecarboxamide
13242-92-7P 13515-65-6P, Thioisobutyramide 14294-10-1P,
4-Morpholinecarbothioamide 15536-75-1P 16536-95-1P 20295-34-5P,
Cyclopropanecarbothioamide 32955-21-8P 32955-22-9P 33142-21-1P
39624-97-0P 40398-36-5P, 1-Pyrrolidinecarbothioamide 42202-73-3P,
Cyclopentanecarbothioamide 56012-38-5P 59830-60-3P, Z-Phenylalaninal
79836-78-5P 98019-60-4P, 5-Isoxazolemethanol 98278-52-5P 99805-29-5P
104336-01-8P 110600-55-0P 111138-83-1P 118994-86-8P,
5-Oxazolecarboxaldehyde 126533-95-7P 126533-96-8P 126534-22-3P
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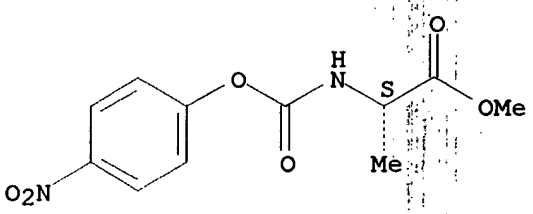
165315-98-0P 165315-99-1P 165316-00-7P 165316-01-8P 165316-02-9P
165316-03-0P 165316-04-1P 165316-05-2P 165316-06-3P 165316-07-4P
165316-08-5P 165316-09-6P 165316-10-9P 165316-11-0P 165316-12-1P
165316-13-2P 165316-14-3P 165316-15-4P 165316-17-6P 165316-18-7P
165316-19-8P 165316-20-1P 165316-21-2P 165316-22-3P 165316-23-4P
165316-24-5P 165316-25-6P 165316-26-7P 165316-27-8P 165316-28-9P
165316-29-0P 165316-30-3P 165316-31-4P 165316-32-5P 165316-33-6P
165316-34-7P 165316-35-8P 165316-36-9P 165316-38-1P 165316-39-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of peptide analogs as retroviral protease inhibitors)

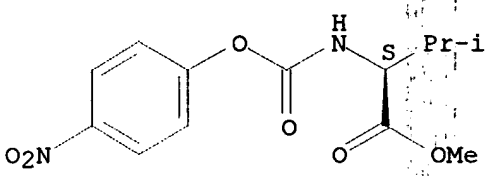
IT **65815-64-7**
RL: RCT (Reactant)
(prepn. of peptide analogs as retroviral protease inhibitors)
RN 65815-64-7 HCAPLUS
CN L-Alanine, N-[(4-nitrophenoxy)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **162537-10-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of peptide analogs as retroviral protease inhibitors)
RN 162537-10-2 HCAPLUS
CN L-Valine, N-[(4-nitrophenoxy)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L27 ANSWER 16 OF 24 HCAPLUS COPYRIGHT 2001 ACS
AN 1995:522611 HCAPLUS
DN 122:291525
TI Retroviral protease inhibiting compounds
IN Norbeck, Daniel W.; Sham, Hing Leung; Kempf, Dale J.; Zhao, Chen
PA Abbott Laboratories, USA
SO PCT Int. Appl., 185 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D263-34
ICS C07D277-587; A61K031-42; A61K031-425
CC 34-2 (**Amino Acids, Peptides,** and **Proteins**)
Section cross-reference(s): 1
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9419332	A1	19940901	WO 1994-US1457	19940208
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5461067	A	19951024	US 1994-185666	19940201
EP 683772	A1	19951129	EP 1994-908018	19940208
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				

	JP 08507061	T2	19960730	JP 1994-519025	19940208
PRAI	US 1993-23226		19930225		
	US 1994-185666		19940201		
	WO 1994-US1457		19940208		

OS MARPAT 122:291525

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Retroviral protease-inhibiting compds. are disclosed, specifically I [R1, R2 = H, (un)substituted alkyl, aryl, alkenyl, heterocyclyl, substituted carbonyl; Y = NHCHR4CO, NHNR4CO, Q1, Q2; Y' = COCHR3NH, CONR3NH, Q3, Q4; a, b = 0-3; c, d = 1-2; R3, R4 = H, (un)substituted alkyl, aryl, alkenyl, heterocyclyl, substituted carbonyl; R3', R4' = H, alkyl; m, n = 0-1; R5, R6 = C(T)GR7; T = O, S; G = CH2, O, S, NR8; R7 = (un)substituted alkyl or cycloalkyl, aryl, protecting group; R8 = H, alkyl, cycloalkyl] and their salts, esters, and prodrugs. For example, 5-(hydroxymethyl)thiazole (prepd. in 4 steps) reacted with 4-nitrophenyl chloroformate to give 78% of the corresponding carbonate. This reacted with 2-(tert-butoxycarbonylamino)-4S-hydroxy-5S-amino-1,6-diphenyl-2-azahexane (prepn. given), followed by deprotection and coupling with a corresponding valine deriv., to give title compd. II. At 0.5 nM in vitro, II gave 77% inhibition of HIV-1 protease. II also gave 50% inhibition of cytopathy of MT4 cells by HIV-13B at 0.10-0.11 .mu.M, with a cellular LC50 of 17.mu.M. Examples include 69 syntheses (some prophetic), and similar biol. data for other selected I.

ST valinyl aminohydroxyazahexane prepn retroviral protease inhibitor; HIV protease inhibitor aminohydroxyazahexane prepn

IT Virucides and Virustats
(prepn. of valinylaminohydroxyazahexane derivs. and analogs as retroviral protease inhibitors)

IT Peptides, preparation
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of valinylaminohydroxyazahexane derivs. and analogs as retroviral protease inhibitors)

IT Virus, animal
(human immunodeficiency, prepn. of valinylaminohydroxyazahexane derivs. and analogs as retroviral protease inhibitors)

IT 144114-21-6, Retropepsin
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(HIV; prepn. of valinylaminohydroxyazahexane derivs. and analogs as retroviral protease inhibitors)

IT 60222-90-4P, 5-Hydroxypentanal oxime 128018-44-0P
RL: BYP (Byproduct); PREP (Preparation)
(byproduct; prepn. of valinylaminohydroxyazahexane derivs. and analogs as retroviral protease inhibitors)

IT 115-08-2P, Thioformamide 934-53-2P, 2-Chloro-2-phenylpropane 13242-92-7P, 4-(Chloromethyl)-2-(dimethylamino)thiazole 13515-65-6P, 2-Methylpropanethioamide 14294-10-1P, 4-(Aminothiocarbonyl)morpholine 15536-75-1P, 2-Methoxythioacetamide 16689-35-3P 24469-50-9P 30293-86-8P, .alpha.-Isocyanatovaline methyl ester 32939-32-5P 32955-22-9P, Ethyl thiazole-5-carboxylate 33142-21-1P, Ethyl 2-chloro-2-formylacetate 38585-74-9P, 5-(Hydroxymethyl)thiazole 39624-97-0P 40398-36-5P, 1-[Amino(thiocarbonyl)]pyrrolidine

41337-78-4P, 2-Carboethoxy-6-ethylpyridine 53370-84-6P 57699-48-6P
57699-55-5P 59830-60-3P, N-Benzyloxycarbonyl-L-phenylalaninal
65386-28-9P, 4-(Chloromethyl)-2-isopropylthiazole hydrochloride
98019-60-4P, 5-(Hydroxymethyl)isoxazole 99805-29-5P 100868-72-2P,
2-[(N-Methylamino)methyl]pyridine dihydrochloride 126533-95-7P, Ethyl
2-(4-morpholinyl)thiazole-4-carboxylate 126533-96-8P,
2-(4-Morpholinyl)-4-(hydroxymethyl)thiazole 134807-06-0P 134807-20-8P
134807-28-6P 134807-29-7P 134807-30-0P 137515-66-3P 144163-45-1P
144163-71-3P 144163-97-3P 144186-53-8P 144186-59-4P 149267-56-1P
149267-64-1P 149267-65-2P 149267-73-2P 150767-00-3P 150767-02-5P
150767-04-7P 150767-05-8P 150767-08-1P 154212-60-9P 154212-61-0P
154248-99-4P 155884-24-5P, Methyl 2-isopropyl-4-oxazolecarboxylate
161852-61-5P **162537-10-2P** 162739-61-9P 162739-62-0P
162739-63-1P 162739-64-2P 162739-65-3P 162739-66-4P 162739-67-5P
162739-71-1P 162739-76-6P 162739-77-7P 162739-78-8P 162739-79-9P
162739-80-2P 162739-81-3P 162739-82-4P 162739-83-5P 162739-84-6P
162739-85-7P 162739-86-8P 162739-93-7P 162739-94-8P,
2-Isopropyl-4-[(N-methylamino)methyl]oxazole 162739-95-9P 162739-96-0P
162739-97-1P, 2-[(N-Methylamino)methyl]-6-ethylpyridine 162739-98-2P,
2-(N,N-Dimethylamino)-4-(hydroxymethyl)thiazole 162739-99-3P, Ethyl
2-(1-pyrrolidinyl)thiazole-4-carboxylate 162740-00-3P,
2-(1-Pyrrolidinyl)-4-(hydroxymethyl)thiazole 162740-01-4P,
4-(Chloromethyl)-2-(methoxymethyl)thiazole hydrochloride 162740-02-5P,
2-(Methoxymethyl)-4-[(N-methylamino)methyl]thiazole 162740-03-6P,
4-Hydroxymethyl-2-isopropyloxazole 163658-33-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(intermediate; prepn. of valinylaminohydroxyazahexane derivs. and analogs as retroviral protease inhibitors)

IT 144163-72-4P 144186-54-9P 162739-68-6P 162739-69-7P 162739-70-0P
162739-72-2P 162739-73-3P 162739-74-4P 162739-75-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(intermediate; prepn. of valinylaminohydroxyazahexane derivs. and analogs as retroviral protease inhibitors)

IT 150767-06-9P 162739-20-0P 162739-24-4P 162739-28-8P 162739-31-3P
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of valinylaminohydroxyazahexane derivs. and analogs as retroviral protease inhibitors)

IT 162739-22-2P 162739-25-5P 162739-26-6P 162739-27-7P 162739-29-9P
162739-30-2P 162739-32-4P
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of valinylaminohydroxyazahexane derivs. and analogs as retroviral protease inhibitors)

IT 150767-07-0P 150767-09-2P 162739-33-5P 162739-35-7P 162739-38-0P
162739-43-7P 162739-46-0P
RL: BAC (Biological activity or effector, except adverse); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of valinylaminohydroxyazahexane derivs. and analogs as retroviral protease inhibitors)

IT 150767-10-5P 162739-21-1P 162739-23-3P 162739-34-6P 162739-36-8P
162739-37-9P 162739-39-1P 162739-40-4P 162739-41-5P 162739-42-6P
162739-44-8P 162739-45-9P 162739-47-1P 162739-48-2P 162739-49-3P
162739-50-6P 162739-51-7P 162739-52-8P 162739-53-9P 162739-54-0P
162739-55-1P 162739-56-2P 162739-57-3P 162739-58-4P 162739-59-5P
162739-60-8P

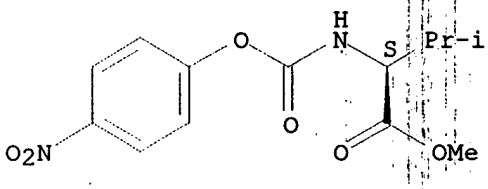
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of valinylaminohydroxyazahexane derivs. and analogs as retroviral protease inhibitors)

IT 67-64-1, Acetone, reactions 70-23-5, Ethyl bromopyruvate 74-89-5, Methylamine, reactions 75-12-7, Formamide, reactions 75-44-5, Carbonic dichloride 98-01-1, 2-Furaldehyde, reactions 98-83-9, .alpha.-Methylstyrene, reactions 100-52-7, Benzaldehyde, reactions 100-55-0, Pyridine-3-methanol 100-83-4, 3-Hydroxybenzaldehyde 105-39-5, Ethyl chloroacetate 109-94-4, Ethyl formate 110-91-8, Morpholine, reactions 122-51-0, Triethyl orthoformate 123-08-0, 4-Hydroxybenzaldehyde 123-11-5, p-Anisaldehyde, reactions 123-75-1, Pyrrolidine, reactions 459-57-4, 4-Fluorobenzaldehyde 498-60-2, 3-Furaldehyde 534-07-6, 1,3-Dichloroacetone 563-83-7, Isobutyramide 586-98-1, Pyridine-2-methanol 591-31-1, m-Anisaldehyde 688-99-3, 3-Hydroxy-5-hexene 870-46-2, tert-Butyl carbazate 872-85-5, Pyridine-4-carboxaldehyde 925-90-6, Ethylmagnesium bromide 930-45-0, (S,S)-2-Aminocyclopentanol 1121-60-4, Pyridine-2-carboxaldehyde 1779-49-3, Triphenylmethylphosphonium bromide 2043-61-0, Cyclohexanecarboxaldehyde 3731-51-9, 2-(Aminomethyl)pyridine 5470-11-1, Hydroxylamine hydrochloride 6089-04-9, 3,4,5,6-Tetrahydro-2-(2-propynyloxy)-2H-pyran 6160-65-2, Thiocarbonyl diimidazole 6306-52-1, L-Valine methyl ester hydrochloride 6372-14-1, N-Benzyloxycarbonyl-L-phenylalaninol 6972-05-0, N,N-Dimethylthiourea 7664-41-7, Ammonia, reactions 7693-46-1, 4-Nitrophenyl chloroformate 14337-43-0, Ethyl chlorooximidoacetate 16332-06-2, 2-Methoxyacetamide 57699-57-7 69353-16-8 74111-21-0, (S,S)-2-Aminocyclohexanol 82625-45-4, 4-(2-Morpholinoethoxy)benzaldehyde 130782-46-6 135941-95-6 135941-97-8 162739-87-9 162739-88-0 162739-89-1 162739-90-4 162739-91-5 162739-92-6 162740-04-7, 4-(Chloromethyl)-2-(dimethylamino)thiazole dihydrochloride 162740-05-8, N-Isobutyrylserine methyl ester
RL: RCT (Reactant)
(reactant; prepn. of valinylaminohydroxyazahexane derivs. and analogs as retroviral protease inhibitors)

IT **162537-10-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(intermediate; prepn. of valinylaminohydroxyazahexane derivs. and analogs as retroviral protease inhibitors)

RN 162537-10-2 HCAPLUS
CN L-Valine, N-[(4-nitrophenoxy)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

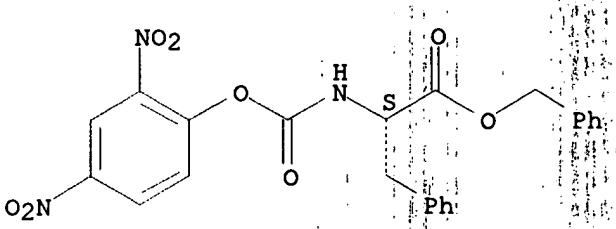


L27 ANSWER 17 OF 24 HCAPLUS COPYRIGHT 2001 ACS
AN 1991:186008 HCAPLUS
DN 114:186008
TI Synthesis and spectroscopic properties of azaglutamine amino acid and peptide derivatives

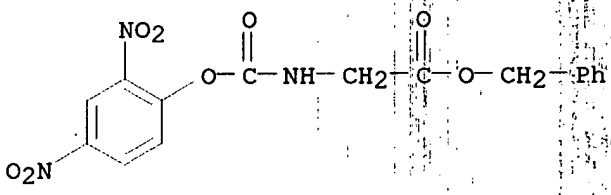
AU Gray, C. J.; Quibell, M.; Jiang, K. L.; Baggett, N.
CS Sch. Chem., Univ. Birmingham, Birmingham, B15 2TT, UK
SO Synthesis (1991), (2), 141-6
CODEN: SYNTBF; ISSN: 0039-7881
DT Journal
LA English
CC 34-3 (**Amino Acids, Peptides,** and **Proteins**)
OS CASREACT 114:186008
AB Azaglutamines H2NCOCH2CH2N(NHBoc)CO2R (Boc = Me3CO2C; R = Et, CH2Ph) were prepd. by treating H2NCOCH2NHNHBOc (I) with ClCO2R. Dipeptides H2NCOCH2CH2N(NHBoc)CO-X-OCH2Ph (X = Gly, Phe) were prepd. by treating I with 2,4-(O2N)C6H3O2C-X-OCH2Ph. I was treated with OCNCH2CO2Et to give H2NCOCH2CH2N(NHBoc)CONHCH2CO2Et.
ST azaglutamine peptide; glutamine aza
IT Peptides, preparation
RL: SPN (Synthetic preparation); PREP (Preparation)
(azaglutamine-contg., prepn. and NMR of)
IT 870-46-2, tert-Butyl carbazate 30189-48-1 41863-52-9
RL: RCT (Reactant)
(addn. reaction of, with acrylamide)
IT 79-06-1, 2-Propenamide, reactions
RL: RCT (Reactant)
(addn. reaction of, with tert-Bu carbazate)
IT 133382-90-8P 133382-91-9P 133382-92-0P 133382-95-3P 133382-96-4P
133382-99-7P 133383-00-3P 133383-04-7P 133383-05-8P 133383-06-9P
133383-07-0DP, derivs.
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and NMR of)
IT 133382-98-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, with Et isocyanatoacetate)
IT 1738-76-7P, Glycine benzyl ester tosylate 1738-78-9P, L-Phenylalanine benzyl ester tosylate
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, with bis(dinitrophenyl) carbonate)
IT 133382-89-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, with chloroformates or Et isocyanoacetafte)
IT 133382-97-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, with dinitrophenoxycarbonyl amino acid esters)
IT **133382-93-1P 133382-94-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, with hydrazide)
IT 133383-19-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
IT 133383-01-4P 133383-02-5P 133383-03-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn., sapon. and NMR of)
IT 501-53-1, Benzyl chloroformate 541-41-3, Ethyl chloroformate 7497-12-3, Bis(2,4-dinitrophenyl) carbonate
RL: RCT (Reactant)
(reaction of, with (tert-butoxycarbonylhydraino)propanamide)
IT 2949-22-6, Ethyl isocyanato acetate
RL: RCT (Reactant)
(reaction of, with hydrazides)
IT **133382-93-1P 133382-94-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)

(prepn. and reaction of, with hydrazide)
RN 133382-93-1 HCAPLUS
CN L-Phenylalanine, N-[(2,4-dinitrophenoxy)carbonyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 133382-94-2 HCAPLUS
CN Glycine, N-[(2,4-dinitrophenoxy)carbonyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



L27 ANSWER 18 OF 24 HCAPLUS COPYRIGHT 2001 ACS
AN 1991:62698 HCAPLUS
DN 114:62698
TI New macrocyclic pseudopeptides containing urethane backbone linkages
AU Wu, Youling; Kohn, Joachim
CS Dep. Chem., Rutgers, State Univ., New Brunswick, NJ, USA
SO J. Am. Chem. Soc. (1991), 113(2), 687-8
CODEN: JACSAT; ISSN: 0002-7863
DT Journal
LA English
CC 34-3 (**Amino Acids, Peptides,** and **Proteins**)
OS CASREACT 114:62698
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The use of urethane bonds as a new type of amide bone mimetic in the design of pseudopeptides was investigated. Urethane backbone linkages were derived from the side chain hydroxyl group of tyrosine by reacting Boc-Tyr-OHex (Boc = Me3CO2C, Hex = hexyl) with p-nitrophenyl chloroformate, followed by reaction with alanine benzyl ester to give urethane-bonded pseudodipeptide I. The resulting Tyr-Ala pseudodipeptide could be cyclized to 24- and 36-membered macrocyclic pseudopeptides II and III, resp., with cyclization yields of about 80%. The unusual ease with which the Tyr-Ala pseudodipeptide underwent cyclizations is probably a consequence of the cis conformation of the urethane bond. In a phase

transfer expt., the ion binding properties of the 24-membered macrocycle II were studied. II was an effective and selective phase transfer agent for Li+ ions, solubilizing up to 0.6 molar equivalents of Li+ ions in chloroform. The uptake of Na+ and K+ ions was only 0.025 and 0.007 molar equivalents, resp. Since the structure of II can be readily modified, the synthetic approach gives rise to a family of new macrocyclic pseudopeptides.

ST macrocyclic pseudopeptide urethane backbone linkage

IT Alkali metals, reactions
RL: RCT (Reactant)
(binding of, with macrocyclic pseudopeptide contg. urethane backbone linkages)

IT Peptides, preparation
RL: SPN (Synthetic preparation); PREP (Preparation)
(cyclopseudo-, prepn. of, with urethane backbone linkages)

IT 573-83-1 3324-58-1 18390-55-1
RL: PROC (Process)
(binding of, with macrocyclic pseudopeptide contg. urethane backbone linkages)

IT 17831-01-5
RL: RCT (Reactant)
(coupling of, with tyrosine active carbonate deriv.)

IT 131152-83-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and binding of, with alkali metals)

IT 131152-91-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and coupling of, with alanine benzyl ester)

IT **131152-89-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and cyclization of)

IT 131152-86-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and esterification of, with nitrophenol)

IT **131152-87-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and partial deblocking of)

IT 131152-90-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, with nitrophenyl chloroformate)

IT 131152-84-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

IT 131152-85-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn., catalytic transfer hydrogenolysis, and metal-binding properties of)

IT 7693-46-1, p-Nitrophenyl chloroformate
RL: RCT (Reactant)
(reaction of, with tyrosine deriv.)

IT 94326-61-1
RL: RCT (Reactant)
(tert-butoxycarbonylation of)

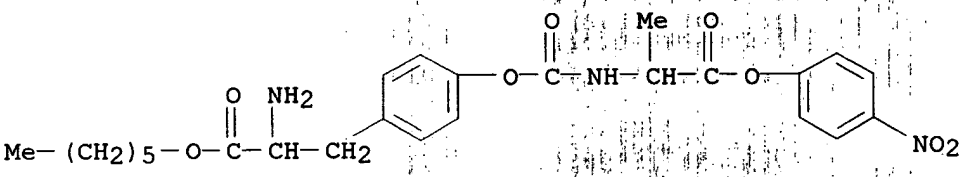
IT **131152-89-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and cyclization of)

RN 131152-89-1 HCAPLUS

CN L-Tyrosine, hexyl ester, ester with N-carboxy-L-alanine 1-(4-nitrophenyl) ester, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

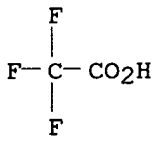
CM 1

CRN 131152-88-0
CMF C25 H31 N3 O8
CDES *

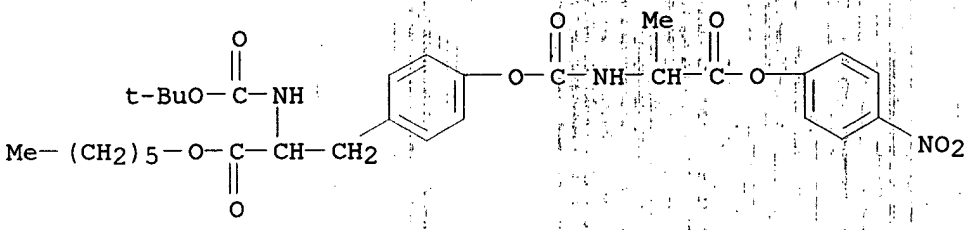


CM 2

CRN 76-05-1
CMF C2 H F3 O2



IT **131152-87-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and partial deblocking of)
RN 131152-87-9 HCAPLUS
CN L-Tyrosine, N-[(1,1-dimethylethoxy)carbonyl]-, hexyl ester, ester with N-carboxy-L-alanine 1-(4-nitrophenyl) ester (9CI) (CA INDEX NAME)



L27 ANSWER 19 OF 24 HCAPLUS COPYRIGHT 2001 ACS
AN 1990:99261 HCAPLUS
DN 112:99261
TI Preparation of N-(phosphonocyclohexylhydroxypropyl) derivatives of amino acids and dipeptides as renin inhibitors
IN Patel, Dinesh V.
PA Squibb, E. R., and Sons, Inc., USA
SO Eur. Pat. Appl., 121 pp.
CODEN: EPXXDW
DT Patent
LA English
IC ICM C07K005-06

ICS A61K037-64; C07F009-40; C07F009-65; C07F009-32; C07F009-44; A61K031-66

CC 34-3 (**Amino Acids, Peptides, and Proteins**)
Section cross-reference(s): 1

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 331105	A2	19890906	EP 1989-103489	19890228
	EP 331105	A3	19900905		
	R: AT, BE, CH, DE, ES, FR, GB, IT, LI, LU, NL, SE				
	WO 8907940	A1	19890908	WO 1989-US777	19890223
	W: DK, HU, JP				
	HU 52785	A2	19900828	HU 1989-2302	19890223
	JP 02503440	T2	19901018	JP 1989-503323	19890223
	ZA 8901594	A	19891129	ZA 1989-1594	19890301
	AU 8930999	A1	19890907	AU 1989-30999	19890302
	DK 8905469	A	19891227	DK 1989-5469	19891102
	US 5217958	A	19930608	US 1990-509398	19900412
PRAI	US 1988-163593		19880303		
	WO 1989-US777		19890223		
	US 1989-317257		19890228		

OS MARPAT 112:99261

AB Amino acid and dipeptide derivs. X-Y-(CHR5CONH)rCHR4CONHCHR3CH(OH)P(:M)(Z1R2)ZR1 [I; M = O, S; Y = CH2, NH, O; when Y = CH2, X = N-(substituted alkyl)carbamoyl or -sulfamoyl, substituted alkanoyl, alkoxycarbonyl, alkylthio, alkanoylthio, etc.; when Y = O, X = N-(substituted alkyl)carbamoyl, substituted alkanoyl, alkoxycarbonyl, phosphono, etc.; when Y = NH, X = N-(substituted alkyl)carbamoyl, substituted alkoxycarbonyl, alkanoyl, alkyl, alkylthio, etc.; R1, R2 = H, (cyclo)alkyl, arylalkyl, (hetero)aryl; Z, Z1 = bond, (un)substituted CH2, NH, cyclic amino, heterocyclyl; R3, R5 = H, lower (halo)alkyl, arylalkyl, heterocyclylalkyl, cycloalkyl, (CH2)nOH, (CH2)nNH2, (CH2)nSH, (CH2)nNHC(:NH)NH2, (CH2)nCONH2, N-substituted 5-imidazolylalkyl, etc.; R4 = any group defined for R3 and R5, N-substituted 2-imidazolyl, 4- or 2-thiazolylalkyl, 3-pyrazolylalkyl, 4- or 2-oxazolylalkyl; n = 1-5], useful as cardiovascular agents in the treatment of hypertension, congestive heart failure, renin-dependent hyperaldosteronism, myocardial infarction, etc., and as a diagnostic agent in detg. renin related disorders (no data), were prepd. I are also inhibitors of retroviral protease and thus are useful as virucides against human T-cell leukemia virus HTLV-1 and HTLV-III (no data). Thus, hydrogenation of (S)-BOC-Phe-OH (BOC = Me3CO2C) over PtO2 and amidation of the resulting (S)-BOC-NHCHQCO2H (Q = cyclohexylmethyl) with MeNHOMe.HCl in THF contg. carbodiimidazole gave (S)-BOC-NHCHQCONMeOMe. Redn. of the latter with LiAlH4 in THF/Et2O at 0.degree. to (S)-BOC-NHCHQCHO followed by addn. reaction with (MeO)2PH in DMF in the presence of KF gave a 12.7:1.0 diastereomeric mixt. of (1S)-BOC-NHCHQCH(OH)P(OMe)2 (Q unchanged). N-Deprotection of the latter with 1.2 N HCl in EtOAc and condensation with BOC-Leu-OH.H2O in DMF in the presence of hydroxybenzotriazole, Et3N, and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide-HCl gave a major diastereomer (1S)-BOC-Leu-NHCHQCH(OH)P(OMe)2. Approx. 25 I were prepd.

ST amino acid phosphonocyclohexylhydroxypropyl renin inhibitor; peptide phosphonocyclohexylhydroxypropyl prepn renin inhibitor; cardiovascular agent phosphonocyclohexylhydroxypropyl dipeptide amide; antihypertensive phosphonocyclohexylhydroxypropyl dipeptide amide

IT Aldosteronism
(treatment of, N-(phosphonohydroxyalkyl)amino acids and -dipeptides for)

IT Antihypertensives

Cardiovascular agents
Virucides and Virustats
(N-(phosphonohydroxyalkyl)amino acid and -dipeptide amides)

IT Amides
RL: SPN (Synthetic preparation); PREP (Preparation)
(amino, N-(phosphonohydroxyalkyl), prepn. of, as renin inhibitors and cardiovascular agents)

IT Peptides, compounds
RL: SPN (Synthetic preparation); PREP (Preparation)
(di-, amides, N-(phosphonohydroxyalkyl), prepn. of, as renin inhibitors and cardiovascular agents)

IT Heart
(failure, treatment of, N-(phosphonohydroxyalkyl)amino acids and -dipeptides for)

IT Heart, disease or disorder
(infarction, treatment of, N-(phosphonohydroxyalkyl)amino acids and -dipeptides for)

IT 3587-60-8
RL: RCT (Reactant)
(N-alkylation by, of histidine Me ester deriv.)

IT 7693-46-1, p-Nitrophenyl chloroformate
RL: RCT (Reactant)
(acylation by, of Me phenylalaninate)

IT 501-53-1, Benzyl chloroformate
RL: RCT (Reactant)
(acylation by, of aminocaproic acid)

IT 108-23-6, Isopropyl chloroformate 1070-83-3, tert-Butylacetic acid
RL: RCT (Reactant)
(acylation by, of histidinamide deriv.)

IT 24424-99-5, Di-tert-Butyl dicarbonate
RL: RCT (Reactant)
(acylation by, of histidine Me ester)

IT 645-45-4, Hydrocinnamoyl chloride
RL: RCT (Reactant)
(acylation by, of leucine)

IT 3400-45-1, Cyclopentanecarboxylic acid
RL: RCT (Reactant)
(acylation by, of phenylalanylleucinamide)

IT 60-32-2
RL: RCT (Reactant)
(acylation of, by benzyl chloroformate)

IT 7524-50-7, L-Phenylalanine methyl ester hydrochloride
RL: RCT (Reactant)
(acylation of, by cyclopentanecarboxylic acid)

IT 61-90-5, L-Leucine, reactions
RL: RCT (Reactant)
(acylation of, by hydrocinnamoyl chloride)

IT 762-04-9 868-85-9, Dimethyl phosphite
RL: RCT (Reactant)
(addn. reaction of, with aminocyclohexylpropanal deriv.)

IT 75-26-3, 2-Bromopropane 78-77-3, 1-Bromo-2-methylpropane
RL: RCT (Reactant)
(alkylation by, of [(hydroxymethoxyphosphinyl)ethyl]oxazolidinecarboxylate)

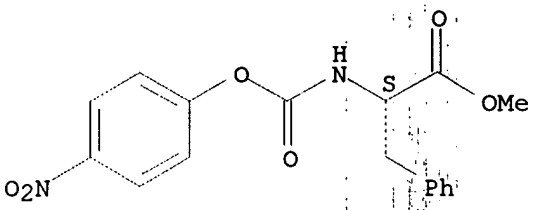
IT 25024-53-7
RL: RCT (Reactant)
(amidation of, with (aminophenyl)phosphonate deriv.)

IT 2018-66-8
RL: RCT (Reactant)
(amidation of, with (aminopropyl)phosphonate deriv.)

IT 110-91-8, Morpholine, reactions
RL: RCT (Reactant)
(amidation of, with Me [(nitrophenoxy)carbonyl]phenylalaninate)
IT 6638-79-5, O,N-Dimethylhydroxylamine hydrochloride
RL: RCT (Reactant)
(amidation of, with aminocyclohexylpropanoic acid deriv.)
IT 501-52-0, Hydrocinnamic acid
RL: RCT (Reactant)
(amidation of, with leucinamide deriv.)
IT 74-89-5, Methylamine, reactions
RL: RCT (Reactant)
(amination by, of (hydroxymethoxyphosphinyl)oxazolidinecarboxylate)
IT 13139-15-6
RL: RCT (Reactant)
(condensation of, with di-Me (aminocyclohexylhydroxypropyl)phosphonate)
IT 71-00-1, L-Histidine, reactions
RL: RCT (Reactant)
(conversion of, to Me ester)
IT 77-76-9, 2,2-Dimethoxypropane
RL: RCT (Reactant)
(cyclocondensation of, with [(cyclohexylmethyl)hydroxyethyl]carbamate deriv.)
IT 1498-40-4, Ethyl dichlorophosphine
RL: RCT (Reactant)
(esterification of, with methanol)
IT 13734-34-4
RL: RCT (Reactant)
(hydrogenation of)
IT 9015-94-5, Renin, uses and miscellaneous
RL: USES (Uses)
(inhibitors, N-(phosphonocyclohexylhydroxypropyl)amino acids and dipeptides)
IT 75-16-1, Methylmagnesium bromide
RL: RCT (Reactant)
(methylation by, of [(hydroxymethoxyphosphinyl)ethyl]oxazolidinecarboxylate)
IT 2666-93-5
RL: RCT (Reactant)
(peptide coupling of, in prepn. of renin inhibitor)
IT 1947-00-8P 2752-56-9P 15027-08-4P 20898-43-5P 22888-60-4P,
L-Histidine methyl ester hydrochloride 27852-48-8P 33014-68-5P
37736-82-6P 38155-45-2P **54601-21-7P** 64152-76-7P
64155-03-9P 75691-91-7P 83468-82-0P 83468-83-1P 98105-42-1P
111629-40-4P 114457-62-4P 114473-20-0P 115766-13-7P 120915-52-8P
120915-53-9P 121533-66-2P 125399-33-9P 125399-34-0P 125399-35-1P
125399-36-2P 125399-37-3P 125399-38-4P 125399-39-5P 125399-40-8P
125399-41-9P 125399-42-0P 125399-43-1P 125399-44-2P 125399-45-3P
125399-46-4P 125399-47-5P 125399-48-6P 125399-49-7P 125399-50-0P
125399-51-1P 125399-52-2P 125399-53-3P 125399-54-4P 125399-55-5P
125399-56-6P 125399-57-7P 125399-58-8P 125399-59-9P 125399-60-2P
125435-73-6P 125435-74-7P 125435-75-8P 126431-13-8P 126431-14-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for renin inhibitor and cardiovascular agent)
IT 125399-09-9P 125399-10-2P 125399-12-4P 125399-13-5P 125399-14-6P
125399-15-7P 125399-16-8P 125399-17-9P 125399-19-1P 125399-20-4P
125399-21-5P 125399-22-6P 125399-23-7P 125399-24-8P 125399-25-9P
125399-26-0P 125399-27-1P 125399-28-2P 125399-29-3P 125399-30-6P
125399-31-7P 125399-32-8P 125435-72-5P 125472-49-3P
RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. of, as renin inhibitor and cardiovascular agent)
IT 75-77-4, Trimethylsilyl chloride, reactions
RL: RCT (Reactant)
(silylation by, of [(cyclohexylmethyl)(ethylmethoxyphosphinyl)hydroxy ethyl]carbamate)
IT **54601-21-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for renin inhibitor and cardiovascular agent)
RN 54601-21-7 HCAPLUS
CN L-Phenylalanine, N-[(4-nitrophenoxy)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

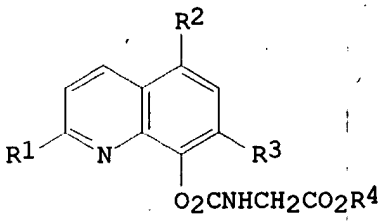
Absolute stereochemistry.



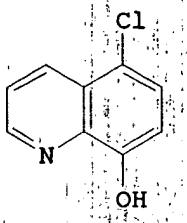
L27 ANSWER 20 OF 24 HCAPLUS COPYRIGHT 2001 ACS
AN 1985:7099 HCAPLUS
DN 102:7099
TI 8-Quinolinyl carbamates and their use as urinary tract antimicrobials
IN Paxton, Larry D.; Madison, Rita A.; Dunbar, Joseph E.
PA Dow Chemical Co., USA
SO U.S., 6 pp.
CODEN: USXXAM
DT Patent
LA English
IC A61K031-47; C07D215-34
NCL 424258000
CC 34-3 (**Amino Acids, Peptides,** and **Proteins**)
Section cross-reference(s): 10, 27
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 4472404	A	19840918	US 1982-408292	19820816

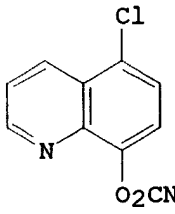
GI



I



II



III

AB Title compds. I (R1 = H, alkyl; R2 = H, NO2, halo; R3 = H, halo; R4 = alkyl) were prepd. as title agents. Thus, quinoline II was treated with Et isocyanoacetate in refluxing EtCOMe contg. Bu2Sn dilaurate to give glycinate III. III was active against Bacillus subtilus with a min. inhibitory concn. 10 ppm.

ST quinolinyl carbamate prepn urinary antimicrobial; glycine quinolinyloxycarbonyl prepn antimicrobial; bactericide quinolinyl carbamate; fungicide quinolinyl carbamate

IT Bactericides, Disinfectants, and Antiseptics
Fungicides and Fungistats
(quinolinyl carbamates)

IT Urinary tract
(quinolinyl carbamates as antimicrobials for)

IT 19498-91-0P 51203-25-9P 93775-51-0P 93775-52-1P 93775-53-2P
93775-54-3P **93775-55-4P** 93775-56-5P 93775-57-6P
93775-58-7P 93775-59-8DP, derivs.
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and antimicrobial activity of)

IT 93775-51-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and hydrolysis and antimicrobial activity of)

IT 19642-75-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

IT 130-16-5 521-74-4 773-76-2 826-81-3 4008-48-4
RL: RCT (Reactant)
(reaction of, with Et isocyanatoacetate)

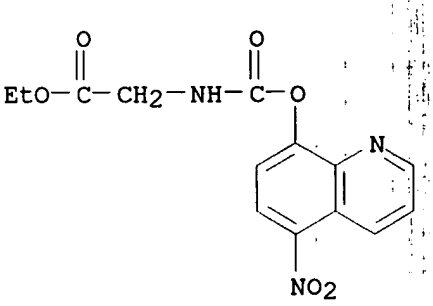
IT 1943-83-5
RL: RCT (Reactant)
(reaction of, with chlorohydroxyquinoline)

IT 2949-22-6
RL: RCT (Reactant)
(reaction of, with hydroxyquinolines)

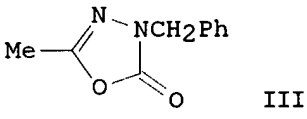
IT **93775-55-4P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and antimicrobial activity of)

RN 93775-55-4 HCAPLUS

CN Glycine, N-[[(5-nitro-8-quinolinyl)oxy]carbonyl]-, ethyl ester (9CI) (CA INDEX NAME)



L27 ANSWER 21 OF 24 HCAPLUS COPYRIGHT 2001 ACS
AN 1977:568362 HCAPLUS
DN 87:168362
TI Preparation and properties of some .alpha.-aza-amino-acid derivatives, their possible use in peptide synthesis
AU Gray, C. J.; Ireson, J. C.; Parker, R. C.
CS Dep. Chem., Univ. Birmingham, Birmingham, Engl.
SO Tetrahedron (1977), 33(7), 739-43
CODEN: TETRAB
DT Journal
LA English
CC 34-2 (Synthesis of **Amino Acids, Peptides,** and **Proteins**)
Section cross-reference(s): 28
GI

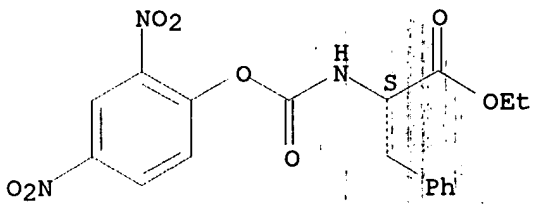


III

AB Azaglycine and azaphenylalanine derivs. were prepd. by acylation of acylhydrazides with alkyl and aryl chloroformates. E.g., Me3CO2CNHNH2 and AcNHNHCH2Ph with ClCO2Ph gave Me3CO2CNHNHCO2Ph (I) and AcNHN(CH2Ph)CO2Ph (II), resp. Esters of acetyl- and benzoylazaamino acids underwent rapid cyclization to oxadiazolones and were unsuitable for peptide synthesis. E.g., II gave the oxadiazolone III on treatment with NaOH or NH2OH or incubation at pH 7 at 37.degree. for several days. Me3CO2CNHNHCON3, prepd. from I by sequential reactions with NH2NH2 and amyl nitrite was too unreactive for peptide synthesis. Coupling reaction of 2,4-dinitrophenyloxycarbonylphenylalanine Et ester with BzNHNH2 and AcNHNH2CH2Ph gave benzoylazaglycyl-L-phenylalanine Et ester and acetylazaphenylalanyl-L-phenylalanine Et ester, resp.
ST aza amino acid prepn cyclization; hydrazide acyl acylation; aza peptide; ring closure aza amino acid; oxadiazolone
IT Amino acids, preparation
RL: SPN (Synthetic preparation); PREP (Preparation)
(aza-, prepn. of, by acylation of hydrazides)
IT Ring closure and formation
(of aza amino acids, oxadiazolones by)
IT Hydrazides
RL: RCT (Reactant)

(acyl, acylation of, aza amino acids by)
IT Peptides, preparation
RL: SPN (Synthetic preparation); PREP (Preparation)
(aza-, prepn. of, by reaction of peptides with acylhydrazides)
IT 613-94-5 870-46-2 1215-52-7 7151-53-3 53370-84-6
RL: RCT (Reactant)
(acylation of)
IT 3081-24-1
RL: RCT (Reactant)
(dinitrophenyloxycarbonylation of)
IT 64512-90-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and azidation of)
IT **64512-92-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and condensation reactions of, with benzoylhydrazide and acetylbenzylhydrazine)
IT 53370-82-4P 53370-85-7P 64512-88-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and cyclization of)
IT 64512-91-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, with benzylamine)
IT 1199-02-6P 15081-44-4P 27643-12-5P 52414-76-3P 53370-83-5P
57699-63-5P 57699-88-4P 64512-81-8P 64512-82-9P 64512-83-0P
64512-84-1P 64512-85-2P 64512-86-3P 64512-87-4P 64512-93-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
IT 64512-89-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn., deprotection, and reactions of, with ammonia and hydrazine)
IT **64512-92-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and condensation reactions of, with benzoylhydrazide and acetylbenzylhydrazine)
RN 64512-92-1 HCAPLUS
CN L-Phenylalanine, N-[(2,4-dinitrophenoxy)carbonyl]-, ethyl ester (9CI) (CA INDEX NAME)

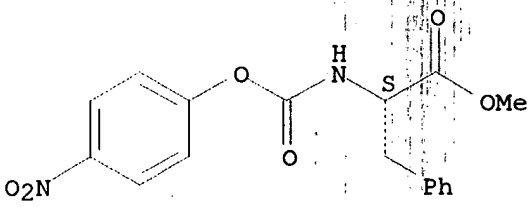
Absolute stereochemistry.



L27 ANSWER 22 OF 24 HCAPLUS COPYRIGHT 2001 ACS
AN 1975:4556 HCAPLUS
DN 82:4556
TI Hydrazine compounds as hetero-components in peptides. XIX. Eledoisin peptides containing the N2-methylcarbazoyl radical (azaalanine)
AU Niedrich, Hartmut; Oehme, Christa; Bergmann, Jutta
CS Zentralinst. Molekularbiol., DAW, Berlin, E. Ger.
SO J. Prakt. Chem. (1974), 316(5), 741-9
CODEN: JPCEAO

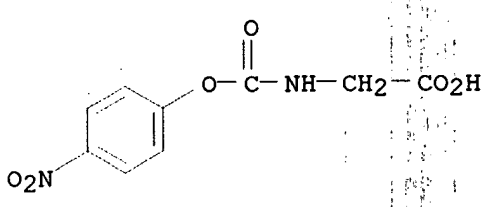
DT Journal
LA German
CC 34-3 (Synthesis of **Amino Acids, Peptides,** and **Pr teins**)
AB Acylation, sapon., and peptide coupling of 2-azaalanine peptides were studied with H2NNMeCONHCHPhCO2Me (Azala-Phe-OMe) (I). 6-Azala-eledoisin sequence 6-11 (II) and 5-Ala-6-Azala-eledoisin 5-11 (III) were prepd. by coupling of I with Ile-Gly-Leu-Met-NH2 in the presence of hydroxysuccinimide and dicyclohexylcarbodiimide. II and III had only the biol. activity of the 7-11 sequence, i.e. .apprx.1% of the 6-11 sequence.
ST azaalanine peptide eledoisin
IT Peptides, preparation
RL: PREP (Preparation)
(azaalanine-contg., eledoisin-related)
IT 3069-69-0
RL: RCT (Reactant)
(methylation of)
IT 40203-94-9
RL: RCT (Reactant)
(peptide coupling reaction with azaalanine derivs.)
IT 2577-90-4
RL: RCT (Reactant)
(peptide coupling reactions of)
IT 1142-20-7 2280-71-9 2304-96-3 2592-19-0 15761-38-3
RL: RCT (Reactant)
(peptide coupling reactions with azaalanine deriv.)
IT 54601-18-2P 54601-22-8P 54601-24-0P 54601-25-1P 54601-26-2P
54601-27-3P 54601-28-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and peptide coupling reactions of)
IT 54601-19-3P 54601-20-6P 54601-23-9P 54601-29-5P 54601-30-8P
54601-31-9P 54601-32-0P 54601-33-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
IT 60-34-4
RL: RCT (Reactant)
(reaction of, with amino acids)
IT 2483-49-0 **54601-21-7**
RL: RCT (Reactant)
(reaction of, with methylhydrazine)
IT **54601-21-7**
RL: RCT (Reactant)
(reaction of, with methylhydrazine)
RN 54601-21-7 HCAPLUS
CN L-Phenylalanine, N-[(4-nitrophenoxy)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

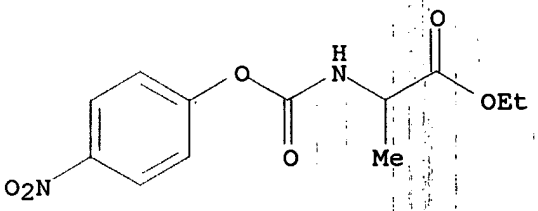


L27 ANSWER 23 OF 24 HCAPLUS COPYRIGHT 2001 ACS

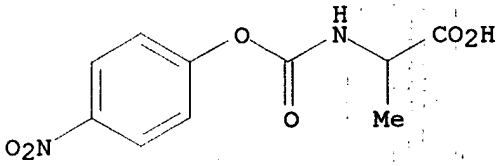
AN 1970:425854 HCAPLUS
DN 73:25854
TI Cyclizations via phenylthio- and phenoxycarbonylamino intermediates. II. Formation of azasuccinic anhydrides and their polycondensation products. Pyridiniocarbonylamino intermediates
AU Baudet, Pierre; Otten, Cl.; Rao, D.
CS Lab. Chim. Org., Univ. Geneve, Geneva, Switz.
SO Helv. Chim. Acta (1970), 53(4), 859-69
CODEN: HCACAV
DT Journal
LA French
CC 34 (Synthesis of **Amino Acids, Peptides,** and **Proteins**)
AB The N-(p-nitrophenoxycarbonyl) derivs. of glycine, DL-alanine and DL-leucine were transformed by pyridine into azasuccinic, 3-methyl-2-azasuccinic and 3-isobutyl-2-azasuccinic anhydride, resp., by way of N-carbamoylpyridinium cation intermediates. The above azasuccinic anhydrides polycondensed in the presence of pyridine yielding the corresponding polyglycine, poly-DL-alanine and poly-DL-leucine, resp. Both cyclization and polycondensation were also catalyzed by .gamma.-collidine, but at a low rate. N-(p-Nitrophenoxycarbonyl)glycine reacted with lysozyme in the presence of pyridine. Several glycine residues were introduced into the enzyme which was rendered insol. and partially inactivated.
ST azasuccinic anhydrides; anhydrides azasuccinic; polyamino acids; lysozyme glycyl; glycyllysozyme
IT Pyridinium compounds
RL: SPN (Synthetic preparation); PREP (Preparation)
(carbonyl derivs. of amino acids, intermediates in oxazolidinedione prepn.)
IT 2,5-Oxazolidinedione, derivs.
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, from phenoxycarbonyl amino acids and pyridine)
IT 1192-73-0P 2185-00-4P 4289-99-0P **21639-02-1P** 25281-63-4P
25718-94-9P 25734-27-4P 25988-64-1P 26283-00-1P 26334-33-8P
26952-07-8P **27317-15-3P** **27317-16-4P** 27317-17-5P
27317-18-6P **27317-19-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
IT **21639-02-1P** **27317-15-3P** **27317-16-4P**
27317-18-6P **27317-19-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 21639-02-1 HCAPLUS
CN Glycine, N-carboxy-, N-(p-nitrophenyl) ester (8CI) (CA INDEX NAME)



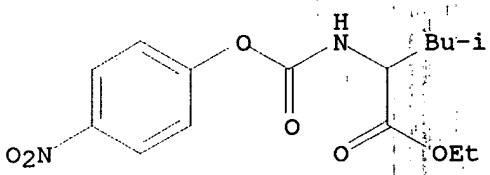
RN 27317-15-3 HCAPLUS
CN Alanine, N-carboxy-, ethyl N-(p-nitrophenyl) ester, DL- (8CI) (CA INDEX NAME)



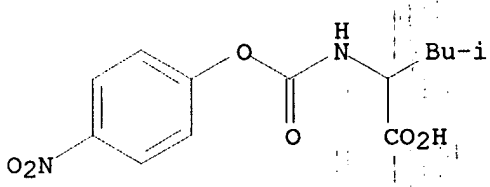
RN 27317-16-4 HCAPLUS
CN Alanine, N-carboxy-, N-(p-nitrophenyl) ester, DL- (8CI) (CA INDEX NAME)



RN 27317-18-6 HCAPLUS
CN Leucine, N-carboxy-, ethyl N-(p-nitrophenyl) ester, DL- (8CI) (CA INDEX NAME)



RN 27317-19-7 HCAPLUS
CN Leucine, N-carboxy-, N-(p-nitrophenyl) ester, DL- (8CI) (CA INDEX NAME)



L27 ANSWER 24 OF 24 HCAPLUS COPYRIGHT 2001 ACS
AN 1967:18854 HCAPLUS
DN 66:18854
TI Peptide syntheses. XXXII. .gamma.-Hydroxyisocaproyl and 3-nitrophenoxycarbonyl moieties as protecting groups
AU Wieland, Theodor; Lamperstorfer, Ch.; Birr, Christian
CS Univ. Frankfurt/M., Frankfurt/M., Ger.
SO Makromol. Chem. (1966), 92, 277-86
CODEN: MACEAK
DT Journal
LA German
CC 34 (Synthesis of **Amino Acids**, **Peptides**, and **Proteins**)

AB cf. CA 64, 14272g. The title protecting groups were found to react readily with various amino acids, and to be removed quant. by CF_3CO_2H treatment and irradiation with uv light (.lambda. >290 m.mu.), resp. Thus, a soln. of 15 g. glycine (I) in 100 ml. 2N NaOH was evapd. to dryness in vacuo and the residue dried in a desiccator. The resulting glycine Na salt (9.7 g.) was pulverized and dissolved in 100 g. molten imidazole (II) on a boiling water bath. Isocaprolactone (16 g.) prepd. according to Stevens and Tarbell (CA 50, 937e) was added, the mixt. was heated 1 hr., cooled, and washed several times with Me_2CO to give 43% N-(.gamma.-hydroxyisocaproyl)glycine (III) Na salt, mixed with a little I Na salt. The crude salt (4.2 g.) was dissolved in 10 ml. H_2O, cooled in ice, acidified to pH 2.6 with 0.1N H_2SO_4, satd. with NaCl, and extd. with five 10 ml. vols. AcEt. The org. exts. were evapd. to a vol. of 20 ml. and treated with petr. ether to give 1.6 g. III, m. 106.degree. (AcOEt-petr. ether). In a similar fashion, N-(.gamma.-hydroxy-isocaproyl)-L-leucine (IV), which sintered at 190.degree. (decompn.), was prepd. in 10% yield. A mixt. of 600 mg. III and L-leucine Me ester hydrochloride was converted by the anhydride method of Determann, et al. (CA 57, 9948c) to N-(.gamma.-hydroxyisocaproyl)-glycyl-L-leucine Me ester in 36% yield. In a similar manner, 390 mg. IV and L-tyrosine benzyl ester tosylate were converted to 50% N-(.gamma.-hydroxyisocaproyl)-L-leucyl-L-tyrosine benzyl ester (V), m. 154-5.degree.. Total hydrolysis of V gave equal amts. leucine (VI) and tyrosine. The .gamma.-hydroxyisocaproyl group was found most difficult to remove in the case of V, 10 mg. of which was dissolved in 0.2 ml. 50% CF_3CO_2H soln., kept 12 hrs. at room temp., and evapd. in a desiccator over concd. H_2SO_4 and KOH. The residue was shown by electrophoresis to be L-leucyl-L-tyrosine benzyl ester. For the prepn. of 3-nitrophenoxycarbonyl derivs., 38 g. $COCl_2$ was dissolved in 160 ml. ice-cold abs. C_6H_6. The soln. was stirred, treated dropwise during 2 hrs. with a soln. of 30 g. m-$O_2NC_6H_4OH$ (VII) and 36.5 g. $PhNMe_2$ in AcOEt at 5-10.degree., and stirred 12 hrs. at room temp. The mixt. was extd. 3 times with 100-ml. vols. N HCl, washed with 100 ml. H_2O, and the org. phase was evapd. to dryness in vacuo to give 74% 3-$O_2NC_6H_4O_2CCl$ (VIII), b13 150-1.degree.. A mixt. of 6.5 g. VI, 4 g. MgO, 100 ml. H_2O, and 30 ml. Et_2O was cooled in ice, stirred vigorously, and treated during 30 min. with a mixt. of 10 g. VIII dild. with an equal vol. Et_2O. The mixt. was acidified with 30 ml. concd. H_2SO_4 and extd. with three 30-ml. vols. AcOEt. The combined org. exts. were washed 3 times with 20-ml. vols. 2N HCl and 5 times with 20-ml. vols. H_2O, dried, and evapd. to dryness in vacuo at 30.degree. to give 62% 3-nitrophenoxycarbonyl-L-leucine, mixed with some VII. In a similar fashion, L-phenylalanine (IX) was converted to 52% 3-nitrophenoxycarbonyl deriv. (X), m. 118.degree. (AcOEt-petr. ether). A soln. of 3.3 g. X and 0.89 g. $NH_2CH_2CO_2Me$ in 50 ml. abs. tetrahydrofuran (XI) was cooled to -15.degree., stirred, and treated with 0.92 ml. $POCl_3$, followed at once by 2.8 ml. Et_3N. The mixt. was stirred 1 hr. at -15.degree., treated with 20 ml. H_2O, and concd. in vacuo. The residue was extd. with three 10-ml. vols. AcOEt, which exts. were combined and washed with 10 ml. H_2O, 10 ml. 5% aq. $NaHCO_3$, and three 10-ml. vols. H_2O, dried, and evapd. to dryness in vacuo at 30.degree. to give 32.5 g. 3-nitrophenoxycarbonyl-L-phenylalanylglycine Me ester, m. 162.degree. (AcOEt-petr. ether and MeOH-H_2O), still mixed with VII. Et_3N (1.43 ml.) and then 0.95 ml. $ClCO_2Et$ was added with shaking to a soln. of 3.3 g. X in 20 ml. XI, and the mixt. cooled to -15.degree.. After 8 min., the mixt. was warmed to 0.degree., treated with a soln. of 2.7 g. L-alanylglycine benzyl ester hydrochloride in 30 ml. XI and 20 ml. H_2O (mixed just before addn. with 1.43 ml. Et_3N), and removed from the cooling bath and shaken until there was a strong evolution of CO_2. The soln. was evapd. in vacuo at 40.degree., and the residue mixed with 60 ml. AcOEt, which phase was washed with two 10-ml. vols. each of N HCl and H_2O, two vols. 5% aq. $NaHCO_3$, and five 10-ml. vols. H_2O, dried, and evapd. in vacuo at

30.degree. to give 75% 3-nitrophenoxycarbonyl-L-phenylalanylglycyl-L-alanine benzyl ester, m. 180-1.degree. (MeOH-H2O). The photolysis of X was performed by irradiating a soln. of 0.98 g. X in 200 ml. 25% aq. XI with a water-cooled high-pressure-Hg lamp (Hanau Q 81). Paper electrophoresis showed hydrolysis to be complete after 4 hrs., and 89% IX was recovered. Expts. to cleave the 3-nitrophenoxy-carbonyl group with aq. Et3N led to hydantoin formation. 18 references.

ST NITROPHENOXYCARBONYL PEPTIDE PROTECTIVE GROUP; HYDROXYISOCAPROYL PEPTIDE PROTECTING GROUPS; PEPTIDE PROTECTING GROUPS HYDROXYISOCAPROYL; NITROPHENOXYCARBONYL PEPTIDE PROTECTIVE GROUP; PEPTIDE PROTECTING GROUPS HYDROXYISOCAPROYL; HYDROXYISOCAPROYL PEPTIDE PROTECTING GROUPS

IT Peptides, preparation
RL: PREP (Preparation)
(4-hydroxy-4-methylvaleryl group and (m-nitrophenoxy)carbonyl group as protective groups for amino group in)

IT Amino group
(4-hydroxy-4-methylvaleryl group and (m-nitrophenoxy)carbonyl group as protective groups for amino group in peptide prepn.)

IT (m-Nitrophenoxy)carbonyl group
4-Hydroxy-4-methylvaleryl group
(as protective group for amino group in peptide prepn.)

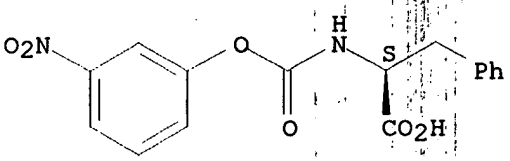
IT 14235-02-0P 14235-03-1P 14235-04-2P 14235-05-3P **14235-06-4P** 14235-07-5P **14235-13-3P** 14317-60-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

IT **14235-06-4P 14235-13-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 14235-06-4 HCAPLUS

CN Alanine, N-carboxy-3-phenyl-, N-(m-nitrophenyl) ester, L- (8CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 14235-13-3 HCAPLUS

CN Leucine, N-carboxy-, N-(m-nitrophenyl) ester, L- (8CI) (CA INDEX NAME)

Absolute stereochemistry.